EAST SEARCH HISTORY

10/706,555

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	("6589947").PN.	USPAT	OR	OFF	2005/11/14 08:11
L2	1	("6043260").PN.	USPAT	OR	OFF	2005/11/14 08:11
L3	1	("5872136").PN.	USPAT	OR	OFF	2005/11/14 08:12
L4	1	("5880140").PN.	USPAT	OR	OFF	2005/11/14 08:12
L5	1	("5883105").PN.	USPAT	OR	OFF	2005/11/14 08:19
L6	911	544/336 — ELECTED SP. HAS THIS CLASS'N.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/11/14 08:20
L7	12	l6 and (crf or corticotropin)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/11/14 08:21

STN SEARCH TRANSCRIPT 10/706,555

```
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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  JUL 20  Powerful new interactive analysis and visualization software,
                  STN AnaVist, now available
 NEWS  4  AUG 11  STN AnaVist workshops to be held in North America
 NEWS  5  AUG 30  CA/CAplus -Increased access to 19th century research documents
 NEWS  6  AUG 30  CASREACT - Enhanced with displayable reaction conditions
 NEWS  7  SEP 09  ACD predicted properties enhanced in REGISTRY/ZREGISTRY
 NEWS  8  OCT 03  MATHDI removed from STN
 NEWS  9  OCT 04  CA/CAplus-Canadian Intellectual Property Office (CIPO) added
                  to core patent offices
 NEWS 10  OCT 06  STN AnaVist workshops to be held in North America
 NEWS 11  OCT 13  New CAS Information Use Policies Effective October 17, 2005
 NEWS 12  OCT 17  STN(R) AnaVist(TM), Version 1.01, allows the export/download
                  of CAplus documents for use in third-party analysis and
                  visualization tools
 NEWS 13  OCT 27  Free KWIC format extended in full-text databases
 NEWS 14  OCT 27  DIOGENES content streamlined
 NEWS 15  OCT 27  EPFULL enhanced with additional content

 NEWS EXPRESS  JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
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Enter NEWS followed by the item number or name to see news on that
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  * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:29:02 ON 14 NOV 2005

=> FILE REG
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                                0.21       0.21

FILE 'REGISTRY' ENTERED AT 08:29:23 ON 14 NOV 2005

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STRUCTURE FILE UPDATES:   13 NOV 2005  HIGHEST RN 867336-65-0
DICTIONARY FILE UPDATES:  13 NOV 2005  HIGHEST RN 867336-65-0

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

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*************************************************************
*                                                           *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                           *
*************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=>
Uploading C:\Program Files\Stnexp\Queries\PYRAZINE CRF ANTAGS MICKELSON.str
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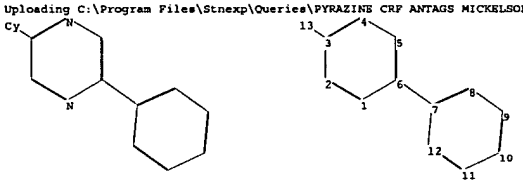


```
chain nodes :
13
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12
chain bonds :
3-13  6-7
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12
exact/norm bonds :
3-13
exact bonds :
6-7
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom
Generic attributes :
13:
Type of Ring System     : Monocyclic

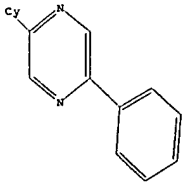


L1      STRUCTURE UPLOADED

=> que L1

L2   QUE L1

=> D L1
L1 HAS NO ANSWERS
L1              STR
```



```
Structure attributes must be viewed using STN Express query preparation.


=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=>
Uploading C:\Program Files\Stnexp\Queries\PYRAZINE CRF ANTAGS MICKELSON TOO.str
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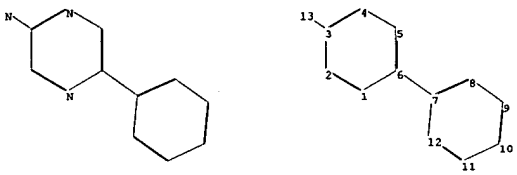


```
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13
chain bonds :
3-13  6-7
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12
exact/norm bonds :
3-13
exact bonds :
6-7
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom



L3      STRUCTURE UPLOADED

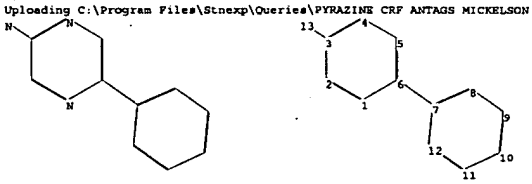
=> que L3

L4   QUE L3

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=>
Uploading C:\Program Files\Stnexp\Queries\PYRAZINE CRF ANTAGS MICKELSON TOO.str
```



```
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13
```

```
chain bonds :
3-13  6-7
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12
exact/norm bonds :
3-13
exact bonds :
6-7
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom

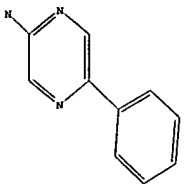


L5      STRUCTURE UPLOADED

=> que L5

L6   QUE L5

=> D L5
L5 HAS NO ANSWERS
L5              STR
```



```
Structure attributes must be viewed using STN Express query preparation.


=> S L1
SAMPLE SEARCH INITIATED 08:31:24 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     1328 TO ITERATE

100.0% PROCESSED     1328 ITERATIONS                                37 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         24374 TO    28746
PROJECTED ANSWERS:              376 TO     1104

L7           37 SEA SSS SAM L1

=> S L1 SSS FULL
FULL SEARCH INITIATED 08:31:29 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     26866 TO ITERATE

100.0% PROCESSED    26866 ITERATIONS                               744 ANSWERS
SEARCH TIME: 00.00.01

L8          744 SEA SSS FUL L1

=> S L8 SUB=L5 SSS FULL
L5 MAY NOT BE USED HERE
The L-number must have been created by a search in this file.  To see
all L-numbers defined in this session, enter DISPLAY HISTORY at an
arrow prompt (=>).  For additional information on subset searching in
this file, enter HELP SUBSET.
ENTER SUBSET L8 OR (END):END
SEARCH ENDED BY USER

=> S L5 SUB=L8 SSS FULL
FULL SUBSET SEARCH INITIATED 08:32:47 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -       121 TO ITERATE

100.0% PROCESSED      121 ITERATIONS                                84 ANSWERS
SEARCH TIME: 00.00.01

L9           84 SEA SUB=L8 SSS FUL L5

=> FILE CAPLUS
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY     SESSION
FULL ESTIMATED COST                              201.53     201.74

FILE 'CAPLUS' ENTERED AT 08:32:53 ON 14 NOV 2005
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FILE LAST UPDATED: 13 Nov 2005  (20051113/ED)

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=> S L9
L10          25 L9

=> D 1-25 IBIB ABS HITSTR

L10  ANSWER 1 OF 25  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:1103771  CAPLUS
DOCUMENT NUMBER:          143:367331
TITLE:                    Pyrazine derivatives as adenosine antagonists, their
                          preparation, pharmaceutical compositions, and use in
                          therapy
INVENTOR(S):              Tsutsumi, Hideo; Tabuchi, Seiichiro; Minagawa,
                          Masatoshi; Akahane, Atsushi
PATENT ASSIGNEE(S):       Astellas Pharma Inc., Japan
SOURCE:                   PCT Int. Appl., 204 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ----------          ----   --------    -------------------    --------
     WO 2005095384        A1    20051013    WO 2005-JP5663         20050322
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
             SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    AU 2004-901772      A  20040401
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

AB   The invention relates to pyrazine derivs. of formula I, which are
     adenosine antagonists.  In compds. I, R is H or (un)substituted lower
     alkyl; X is H, halo, OH, SH, cyano, acyl, (un)substituted lower alkyl,
     (un)substituted lower alkoxy, (un)substituted aryl, etc.; Y is H, halo,
     OH, SH, cyano, acyl, (un)substituted lower alkyl, (un)substituted lower
     alkoxy, (un)substituted lower alkylthio, (un)substituted amino,
     (un)substituted aryl, or (un)substituted heteroaryl; and Z is
     (un)substituted aryl or (un)substituted heteroaryl; or a salt thereof.
     The invention also relates to the preparation of I, pharmaceutical compns.
     containing I, or a pharmaceutically acceptable salt thereof, in admixt. with a
     pharmaceutically acceptable carrier, as well as to the use of the compns.
     in the treatment of disorders responding to adenosine antagonists.  Oxidation
     of 2-isopropyl-6-(phenylethynyl)-3-pyridazinone (II) to the corresponding
     dione followed by condensation with 2,3-diamine-2-butenedinitrile resulted
     in the formation of pyridazinylpyrazine III, which underwent
     regioselective substitution with 4-methoxybenzylamine, debenzylation, and
     hydrolysis to give pyrazinecarboxamide IV.  The amide of IV was cleaved
     followed by decarboxylation, bromination with N-bromosuccinimide, and
     palladium-catalyzed coupling with 5-ethynyl-1-methyl-1H-imidazole to give
     pyrazinylpyridazinone V.  The tested compds. express high affinity for
     adenosine receptors, with compound V expressing Ki values of 0.72 nM and
     0.25 nM for adenosine A1 and A2a receptors, resp.
IT   866264-11-1P, 6-[5-Amino-3-phenyl-6-(1-piperidinyl)-2-pyrazinyl]-2-
     isopropyl-3-pyridazinone  866264-12-2P, 6-[5-Amino-6-[3-
     (dimethylamino)-1-pyrrolidinyl]-3-phenyl-2-pyrazinyl]-2-isopropyl-3-
     pyridazinone  866264-13-3P, 6-[5-Amino-6-(4-methoxy-1-
     piperidinyl)-3-phenyl-2-pyrazinyl]-2-isopropyl-3-pyridazinone
     866264-14-4P, N-[1-[3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-
     pyridazinyl)-5-phenyl-2-pyrazinyl]-4-piperidinyl]methanesulfonamide
     866264-15-5P, 6-[5-Amino-3-phenyl-6-(1-piperazinyl)-2-pyrazinyl]-2-
     isopropyl-3-pyridazinone  866264-16-6P, 6-[5-Amino-6-(4-methyl-1-
     piperazinyl)-3-phenyl-2-pyrazinyl]-2-isopropyl-3-pyridazinone
     866264-17-7P, 6-[5-Amino-3-phenyl-6-[4-(2-pyridylmethyl)-1-
     piperazinyl]-2-pyrazinyl]-2-isopropyl-3-pyridazinone  866264-18-8P,
     6-[5-Amino-3-phenyl-6-(4-phenyl-1-piperazinyl)-2-pyrazinyl]-2-isopropyl-
     3-pyridazinone  866264-19-9P, 6-[5-Amino-6-[4-(4-methoxyphenyl)-1-
     piperazinyl]-3-phenyl-2-pyrazinyl]-2-isopropyl-3-pyridazinone
     866264-20-2P, 6-[6-(4-Acetyl-1-piperazinyl)-5-amino-3-phenyl-2-
     pyrazinyl]-2-isopropyl-3-pyridazinone  866264-33-7P,
     6-[5-Amino-3-phenyl-6-(4-phenyl-1-piperazinyl)-2-pyrazinyl]-2-methyl-3-
     pyridazinone  866264-43-9P, 6-[5-Amino-6-(4-morpholinyl)-3-phenyl-
     2-pyrazinyl]-2-isopropyl-3-pyridazinone  866264-44-0P,
     6-[5-Amino-3-phenyl-6-(1-pyrrolidinyl)-2-pyrazinyl]-2-isopropyl-3-
     pyridazinone  866264-45-1P, 6-[5-Amino-3-phenyl-6-[4-(2-pyridyl)-
     1-piperazinyl]-2-pyrazinyl]-2-isopropyl-3-pyridazinone
     866264-51-9P, 6-[5-Amino-3-phenyl-6-(1H-pyrrol-1-yl)-2-pyrazinyl]-
     2-isopropyl-3-pyridazinone  866264-52-0P, 6-[5-Amino-3-phenyl-6-
     (1H-pyrrol-1-yl)-2-pyrazinyl]-2-methyl-3-pyridazinone  866264-53-1P
     , 6-[5-Amino-3-phenyl-6-(1H-pyrazol-1-yl)-2-pyrazinyl]-2-isopropyl-3-
     pyridazinone  866264-54-2P, 6-[5-Amino-6-(1H-imidazol-1-yl)-3-
     phenyl-2-pyrazinyl]-2-isopropyl-3-pyridazinone  866264-55-3P,
     6-[5-Amino-3-phenyl-6-(1H-1,2,4-triazol-1-yl)-2-pyrazinyl]-2-isopropyl-3-
     pyridazinone  866264-57-5P, 6-[5-Amino-3-phenyl-6-(1H-pyrazol-1-
     yl)-2-pyrazinyl]-2-methyl-3-pyridazinone  866264-58-6P,
     6-[5-Amino-6-(1H-imidazol-1-yl)-3-phenyl-2-pyrazinyl]-2-methyl-3-
     pyridazinone  866264-59-7P, 6-[5-Amino-3-phenyl-6-(1H-1,2,4-
     triazol-1-yl)-2-pyrazinyl]-2-methyl-3-pyridazinone
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (drug candidate; preparation of pyrazine derivs. as adenosine antagonists)
RN   866264-11-1  CAPLUS
CN   3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1-piperidinyl)pyrazinyl]-2-(1-
     methylethyl)- (9CI)  (CA INDEX NAME)
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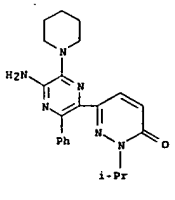

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RN   866264-12-2  CAPLUS
CN   3(2H)-Pyridazinone, 6-[5-amino-6-[3-(dimethylamino)-1-pyrrolidinyl]-3-
     phenylpyrazinyl]-2-(1-methylethyl)- (9CI)  (CA INDEX NAME)
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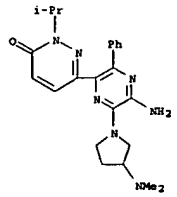
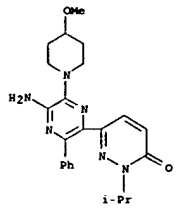
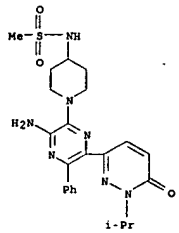


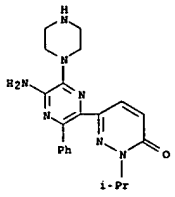
RN 866264-13-3 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-6-(4-methoxy-1-piperidinyl)-3-phenylpyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



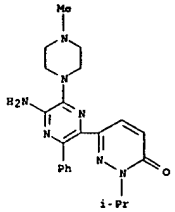
RN 866264-14-4 CAPLUS
CN Methanesulfonamide, N-[1-[3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridazinyl]-5-phenylpyrazinyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



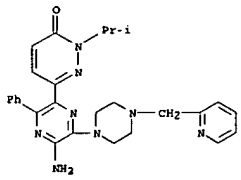
RN 866264-15-5 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1-piperazinyl)pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



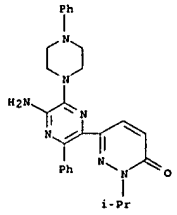
RN 866264-16-6 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-6-(4-methyl-1-piperazinyl)-3-phenylpyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



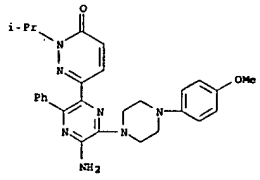
RN 866264-17-7 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-[4-(2-pyridinylmethyl)-1-piperazinyl]pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



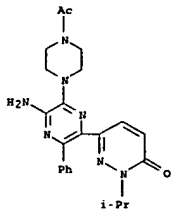
RN 866264-18-8 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(4-phenyl-1-piperazinyl)pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



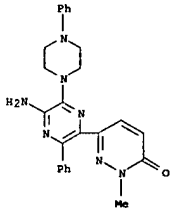
RN 866264-19-9 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-6-[4-(4-methoxyphenyl)-1-piperazinyl]-3-phenylpyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



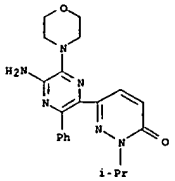
RN 866264-20-2 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



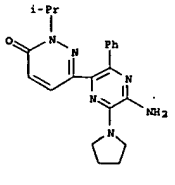
RN 866264-33-7 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(4-phenyl-1-piperazinyl)pyrazinyl]-2-methyl- (9CI) (CA INDEX NAME)



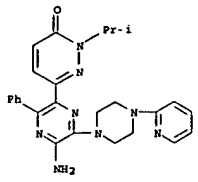
RN 866264-43-9 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-6-(4-morpholinyl)-3-phenylpyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



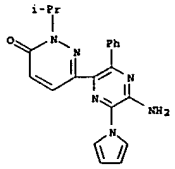
RN 866264-44-0 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1-pyrrolidinyl)pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



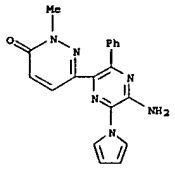
RN 866264-45-1 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-[4-(2-pyridinyl)-1-piperazinyl]pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



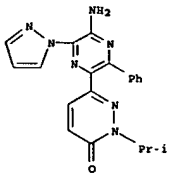
RN 866264-51-9 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1H-pyrrol-1-yl)pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



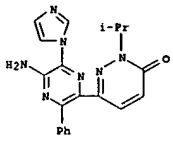
RN 866264-52-0 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1H-pyrrol-1-yl)pyrazinyl]-2-methyl- (9CI) (CA INDEX NAME)



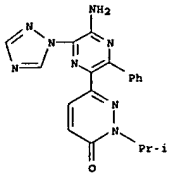
RN 866264-53-1 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1H-pyrazol-1-yl)pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



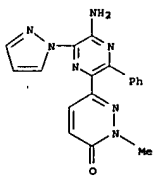
RN 866264-54-2 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-6-(1H-imidazol-1-yl)-3-phenylpyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



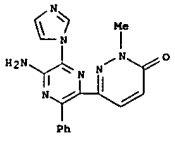
RN 866264-55-3 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



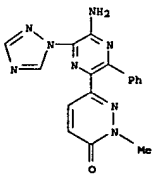
RN 866264-57-5 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1H-pyrazol-1-yl)pyrazinyl]-2-methyl- (9CI) (CA INDEX NAME)



RN 866264-58-6 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-6-(1H-imidazol-1-yl)-3-phenylpyrazinyl]-2-methyl- (9CI) (CA INDEX NAME)



RN 866264-59-7 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1078246 CAPLUS
DOCUMENT NUMBER: 143:367330
TITLE: Pyrazine derivatives as adenosine antagonists, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Tsutsumi, Hideo; Tabuchi, Seiichiro; Minagawa, Masatoshi; Akahane, Atsushi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co. Ltd., Japan
SOURCE: U.S. Pat. Appl. Publ., 54 pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005222159	A1	20051006	US 2005-87761		20050324
PRIORITY APPLN. INFO.:			EP 2004-901772	A	20040401

GI

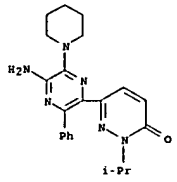
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to pyrazine derivs. of formula I, which are adenosine antagonists. In compds. I, R is H or (un)substituted lower alkyl; X is H, halo, OH, SH, cyano, acyl, (un)substituted lower alkyl, (un)substituted lower alkoxy, (un)substituted aryl, etc.; Y is H, halo, OH, SH, cyano, acyl, (un)substituted lower alkyl, (un)substituted lower alkoxy, (un)substituted lower alkylthio, (un)substituted amino, (un)substituted aryl, or (un)substituted heteroaryl; and Z is (un)substituted aryl or (un)substituted heteroaryl; or a salt thereof. The invention also relates to the preparation of I, pharmaceutical compns. containing I, or a pharmaceutically acceptable salt thereof, in admixt. with a pharmaceutically acceptable carrier, as well as to the use of the compns. in the treatment of disorders responding to adenosine antagonists. Oxidation of 2-isopropyl-6-(phenylethynyl)-3-pyridazinone (II) to the corresponding dione followed by condensation with 2,3-diamine-2-butenedinitrile resulted in the formation of pyridazinylpyrazine III, which underwent regioselective substitution with 4-methoxybenzylamine, debenzylation, and hydrolysis to give pyrazinecarboxamide IV. The amide of IV was cleaved followed by decarboxylation, bromination with N-bromosuccinimide, and palladium-catalyzed coupling with 5-ethynyl-1-methyl-1H-imidazole to give pyrazinylpyridazinone V. The tested compds. express high affinity for adenosine receptors, with compound V expressing Ki values of 0.72 nM and 0.25 nM for adenosine A1 and A2a receptors, resp.

IT 866264-11-1P, 6-[5-Amino-3-phenyl-6-(1-piperidinyl)-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-12-2P, 6-[5-Amino-6-[3-(dimethylamino)-1-pyrrolidinyl]-3-phenyl-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-13-3P, 6-[5-Amino-6-(4-methoxy-1-piperidinyl)-3-phenyl-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-14-4P, N-[1-[3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-phenyl-2-pyrazinyl]-4-piperidinyl]methanesulfonamide 866264-15-5P, 6-[5-Amino-3-phenyl-6-(1-piperazinyl)-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-16-6P, 6-[5-Amino-6-(4-methyl-1-piperazinyl)-3-phenyl-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-17-7P, 6-[5-Amino-3-phenyl-6-[4-(2-pyridylmethyl)-1-piperazinyl]-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-18-8P, 6-[5-Amino-3-phenyl-6-(4-phenyl-1-piperazinyl)-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-19-9P, 6-[5-Amino-6-[4-(4-methoxyphenyl)-1-piperazinyl]-3-phenyl-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-20-2P, 6-[6-(4-Acetyl-1-piperazinyl)-5-amino-3-phenyl-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-33-7P, 6-[5-Amino-3-phenyl-6-(4-phenyl-1-piperazinyl)-2-pyrazinyl]-2-methyl-3-pyridazinone 866264-43-9P, 6-[5-Amino-6-(4-morpholinyl)-3-phenyl-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-44-0P, 6-[5-Amino-3-phenyl-6-(1-pyrrolidinyl)-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-45-1P, 6-[5-Amino-3-phenyl-6-[4-(2-pyridyl)-1-piperazinyl]-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-51-9P, 6-[5-Amino-3-phenyl-6-(1H-pyrrol-1-yl)-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-52-0P, 6-[5-Amino-3-phenyl-6-(1H-pyrrol-1-yl)-2-pyrazinyl]-2-methyl-3-pyridazinone 866264-53-1P

, 6-[5-Amino-3-phenyl-6-(1H-pyrazol-1-yl)-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-54-2P, 6-[5-Amino-6-(1H-imidazol-1-yl)-3-phenyl-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-55-3P, 6-[5-Amino-3-phenyl-6-(1H-1,2,4-triazol-1-yl)-2-pyrazinyl]-2-isopropyl-3-pyridazinone 866264-57-5P, 6-[5-Amino-3-phenyl-6-(1H-pyrazol-1-yl)-2-pyrazinyl]-2-methyl-3-pyridazinone 866264-58-6P, 6-[5-Amino-6-(1H-imidazol-1-yl)-3-phenyl-2-pyrazinyl]-2-methyl-3-pyridazinone 866264-59-7P, 6-[5-Amino-3-phenyl-6-(1H-1,2,4-triazol-1-yl)-2-pyrazinyl]-2-methyl-3-pyridazinone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrazine derivs. as adenosine antagonists)

RN 866264-11-1 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1-piperidinyl)pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 866264-12-2 CAPLUS
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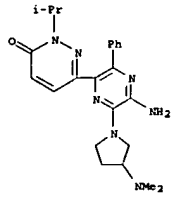
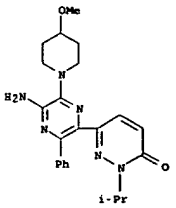
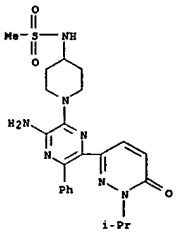


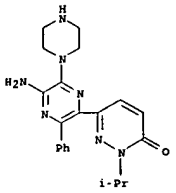
RN 866264-13-3 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-6-(4-methoxy-1-piperidinyl)-3-phenylpyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



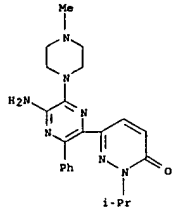
RN 866264-14-4 CAPLUS
CN Methanesulfonamide, N-[1-[3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridazinyl]-5-phenylpyrazinyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



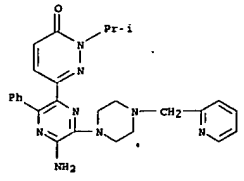
RN 866264-15-5 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1-piperazinyl)pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



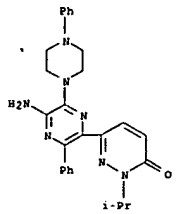
RN 866264-16-6 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-6-(4-methyl-1-piperazinyl)-3-phenylpyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



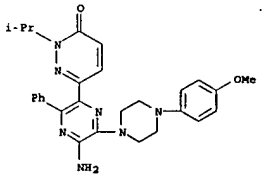
RN 866264-17-7 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-[4-(2-pyridinylmethyl)-1-piperazinyl]pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 866264-18-8 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(4-phenyl-1-piperazinyl)pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 866264-19-9 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-6-[4-(4-methoxyphenyl)-1-piperazinyl]-3-phenylpyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



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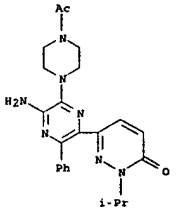
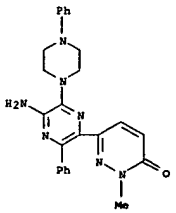


RN 866264-33-7 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(4-phenyl-1-piperazinyl)pyrazinyl]-2-methyl- (9CI) (CA INDEX NAME)



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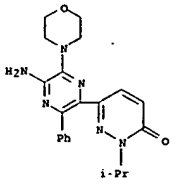
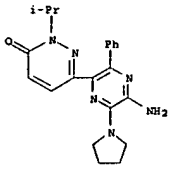
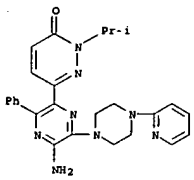
CN 3(2H)-Pyridazinone, 6-[5-amino-6-(4-morpholinyl)-3-phenylpyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 866264-44-0 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1-pyrrolidinyl)pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 866264-45-1 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-[4-(2-pyridinyl)-1-piperazinyl]pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 866264-51-9 CAPLUS
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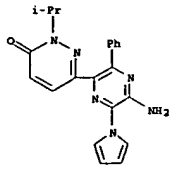
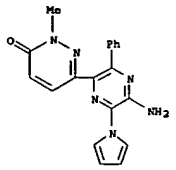
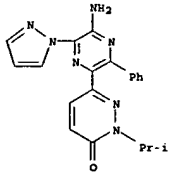


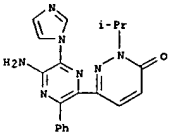
RN 866264-52-0 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1H-pyrrol-1-yl)pyrazinyl]-2-methyl- (9CI) (CA INDEX NAME)



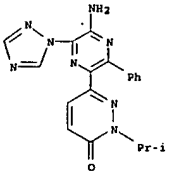
RN 866264-53-1 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1H-pyrazol-1-yl)pyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



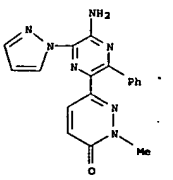
RN 866264-54-2 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-6-(1H-imidazol-1-yl)-3-phenylpyrazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)



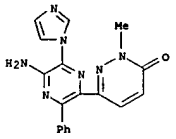
RN 866264-55-3 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



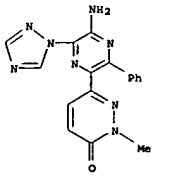
RN 866264-57-5 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-3-phenyl-6-(1H-pyrazol-1-yl)pyrazinyl]-2-methyl- (9CI) (CA INDEX NAME)



RN 866264-58-6 CAPLUS
CN 3(2H)-Pyridazinone, 6-[5-amino-6-(1H-imidazol-1-yl)-3-phenylpyrazinyl]-2-methyl- (9CI) (CA INDEX NAME)



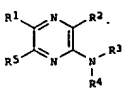
RN 866264-59-7 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



L10 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:450934 CAPLUS
DOCUMENT NUMBER: 143:7731
TITLE: Preparation of pyrazine derivatives as adenosine receptor antagonists for treating neurological, cardiovascular, and other diseases
INVENTOR(S): Yonishi, Satoshi; Aoki, Satoshi; Matsushima, Yuji; Akahane, Atsushi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co. Ltd., Japan
SOURCE: U.S. Pat. Appl. Publ., 37 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005113367	A1	20050526	US 2004-972340		20041026
PRIORITY APPLN. INFO.:			EP 2003-905895	A	20031027
			EP 2004-902764	A	20040524

OTHER SOURCE(S): MARPAT 143:7731
GI

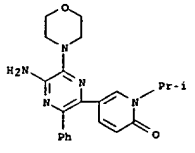


I

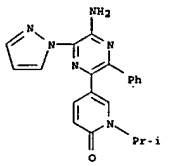
AB Pyrazine derivative of formula I (with variables defined below) or salts thereof are claimed. The pyrazine compound I are adenosine antagonists and are useful for the prevention and/or treatment of depression, dementia (e.g. Alzheimer's disease, cerebrovascular dementia, dementia accompanying Parkinson's disease, etc.), Parkinson's disease, anxiety, pain, cerebrovascular disease (e.g. stroke, etc.), heart failure and the like. A process for preparing the pyrazines and pharmaceutical compns. containing them are also claimed. For I, R1 is substituted pyridin-2-one or pyridine; R2 is H, OH, halogen, cyano, or optionally substituted lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, aryloxy, arylthio, acyl, aryl, heterocyclic group or amino; R3 and R4 are independently H, lower alkyl or acyl; and R5 is optionally substituted lower alkyl, lower alkenyl, lower alkynyl, cyano, aryl or heterocyclic group.

IT 851088-69-2P, 5-[5-Amino-6-(4-morpholinyl)-3-phenyl-2-pyrazinyl]-1-isopropyl-2(1H)-pyridinone 851088-71-6P, 5-[5-Amino-3-phenyl-6-(1H-pyrazol-1-yl)-2-pyrazinyl]-1-isopropyl-2(1H)-pyridinone 851088-72-7P, 5-[5-Amino-3-phenyl-6-(1H-pyrrol-1-yl)-2-pyrazinyl]-1-isopropyl-2(1H)-pyridinone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrazine derivs. as adenosine receptor antagonists for treating neurol., cardiovascular, and other diseases)

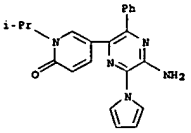
RN 851088-69-2 CAPLUS
CN 2(1H)-Pyridinone, 5-[5-amino-6-(4-morpholinyl)-3-phenylpyrazinyl]-1-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 851088-71-6 CAPLUS
CN 2(1H)-Pyridinone, 5-[5-amino-3-phenyl-6-(1H-pyrazol-1-yl)pyrazinyl]-1-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 851088-72-7 CAPLUS
CN 2(1H)-Pyridinone, 5-[5-amino-3-phenyl-6-(1H-pyrrol-1-yl)pyrazinyl]-1-(1-methylethyl)- (9CI) (CA INDEX NAME)

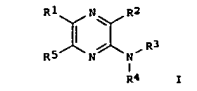


L10 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:395298 CAPLUS
DOCUMENT NUMBER: 142:447235
TITLE: Preparation of pyrazines as adenosine A1 and A2a receptor antagonists and their pharmaceutical compositions
INVENTOR(S): Yonishi, Satoshi; Aoki, Satoshi; Matsushima, Yuji; Akahane, Atsushi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005040151	A1	20050506	WO 2004-JP16193	20041025

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2003-905895 A 20031027
AU 2004-902764 A 20040524
OTHER SOURCE(S): MARPAT 142:447235
GI



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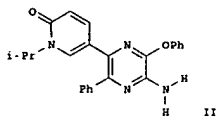
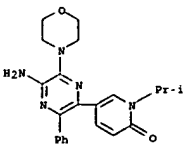


II

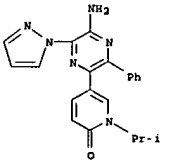
AB Title compound I [wherein R1 = N,3-disubstituted 2(1H)-pyridinonyl, 2-alkoxypyridinyl; R2 = H, OH, halo, CN, (un)substituted lower alk(en/yn)yl, alkoxy, aryloxy, arylthio, acyl, aryl, heterocyclyl or amino; R3, R4 = independently H, lower alkyl, acyl; and their salts] and their salts were prepared as adenosine receptor antagonists. For example, compound II was prepared by etherification of 5-(5-Amino-6-bromo-3-phenyl-2-pyrazinyl)-1-isopropyl-2(1H)-pyridinone (preparation given) with phenol. II showed binding to the human A1 adenosine receptor with Ki = 1.57 nM and to the human A2a adenosine receptor with Ki = 0.32 nM. Thus, I are useful as A1 receptor and A2a receptor dual antagonists and for the prevention and/or treatment of depression, dementia (e.g. Alzheimer's disease, cerebrovascular dementia, dementia accompanying Parkinson's disease, etc.), Parkinson's disease, anxiety, pain, cerebrovascular disease (e.g. stroke, etc.), heart failure and the like (no data).

IT 851088-69-2P, 5-[5-Amino-6-(4-morpholinyl)-3-phenyl-2-pyrazinyl]-1-isopropyl-2(1H)-pyridinone 851088-71-6P, 5-[5-Amino-3-phenyl-6-(1H-pyrazol-1-yl)-2-pyrazinyl]-1-isopropyl-2(1H)-pyridinone 851088-72-7P, 5-[5-Amino-3-phenyl-6-(1H-pyrrol-1-yl)-2-pyrazinyl]-1-isopropyl-2(1H)-pyridinone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrazines as adenosine receptor antagonists)

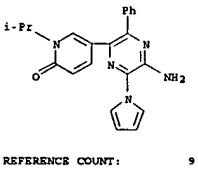
RN 851088-69-2 CAPLUS
CN 2(1H)-Pyridinone, 5-[5-amino-6-(4-morpholinyl)-3-phenylpyrazinyl]-1-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 851088-71-6 CAPLUS
CN 2(1H)-Pyridinone, 5-[5-amino-3-phenyl-6-(1H-pyrazol-1-yl)pyrazinyl]-1-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 851088-72-7 CAPLUS
CN 2(1H)-Pyridinone, 5-[5-amino-3-phenyl-6-(1H-pyrrol-1-yl)pyrazinyl]-1-(1-methylethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:158514 CAPLUS
DOCUMENT NUMBER: 142:261555
TITLE: Preparation of pyrazine derivatives as modulators of cannabinoid receptors
INVENTOR(S): Ellsworth, Bruce A.; Sun, Chongqing; Pendri, Annapurna
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

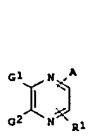
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016286	A2	20050224	WO 2004-US26599	20040816
WO 2005016286	C1	20050414		
WO 2005016286	A3	20050609		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005054659 A1 20050310 US 2004-917199 20040812
PRIORITY APPLN. INFO.: US 2003-495807P P 20030815
US 2004-917199 A 20040812

OTHER SOURCE(S): MARPAT 142:261555
GI



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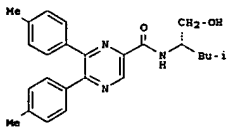
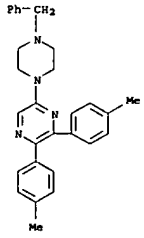


II

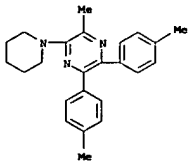
AB The present application describes compds. I [A = CR4R5R6, NR2R3, SR7, S(:O)R8, OR9, (un)substituted heteroaryl; G1, G2 = (un)substituted aryl, (un)substituted heteroaryl; R1 = H, halogen, OH, CN, alkyl, aryl, heteroaryl; R2, R3 = H, alkyl, cycloalkyl, aryl, heterocyclyl, alkoxy, heteroaryl, C(:O)R10, aminoalkyl, iminoalkyl, S(:O)R8,SO2R8; R2R3 = heterocyclyl; R4, R5, R6 = H, alkyl, OH, NR2R3, C(:O)NR2R3, C(:NR2)NR2R3, aryl, heteroaryl; R4R5 = cyclolkyl, heterocyclyl; NR4R5 = imine; R7 = alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl; R8 = alkyl, cycloalkyl, aminoalklyl, aminocycloalkyl, aminoheterocyclyl, aminoaryl, aminoheteroaryl, aryl, heterocyclyl; R9 = aryl, heteroaryl, alkyl, cycloalkyl, heterocyclyl, C(:O)NR2R3; R10 = alkyl, aryl, heteroaryl, alkoxyl, and their stereoisomers and pharmaceutically acceptable salts, useful as modulators of cannabinoid receptors (Ki = 0.01 nM - 13,000 nM). Thus, dicolylpyrazine II was prepared from H2NCH2CH(NH2)CO2H, via esterification with MeOH containing HCl gas, cyclocondensation with 4,4'-dimethylbenzil in MeOH containing KOH, saponification with LiOH in aqueous DMF, chlorination with (COCl)2 in CH2Cl2 containing catalytic DMF and amidation with (S)-(+)-leucinol. Addnl., the present application describes pharmaceutical compns. comprising at least one compound I and optionally one or more addnl. therapeutic agents. Finally, the present application describes methods of treatment using the compds. I both alone and in combination with one or more addnl. therapeutic agents.

IT 845728-72-5P 845728-74-7P 845728-76-9P
845728-77-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazine derivs. as modulators of cannabinoid receptors)

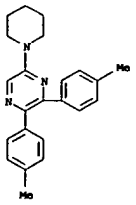
RN 845728-72-5 CAPLUS
CN Pyrazine, 2,3-bis(4-methylphenyl)-5-(1-piperidinyl)- (9CI) (CA INDEX NAME)



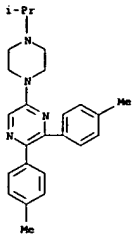
RN 845728-77-0 CAPLUS
CN Pyrazine, 2-methyl-5,6-bis(4-methylphenyl)-3-(1-piperidinyl)- (9CI) (CA INDEX NAME)



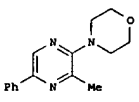
L10 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:763199 CAPLUS
DOCUMENT NUMBER: 141:395500
TITLE: Concise synthesis of 1H-pyrazin-2-ones and 2-aminopyrazines
AUTHOR(S): Adam, Isabelle; Orain, David; Meier, Peter
CORPORATE SOURCE: Lead Synthesis and Chemogenetics, Global Discovery Chemistry, Novartis Institutes for BioMedical Research Basel, Basel, 4056, Switz.
SOURCE: Synlett (2004), (11), 2031-2033
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



RN 845728-74-7 CAPLUS
CN Pyrazine, 5-[4-(1-methylethyl)-1-piperazinyl]-2,3-bis(4-methylphenyl)- (9CI) (CA INDEX NAME)



RN 845728-76-9 CAPLUS
CN Pyrazine, 2,3-bis(4-methylphenyl)-5-[4-(phenylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

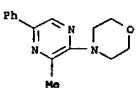


I

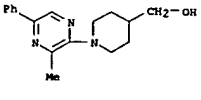
AB Convenient syntheses of 1H-pyrazin-2-ones and 2-aminopyrazines, e.g., I, are described. By coupling Boc-protected amino acids with α-amino ketones or with amino alcs. and subsequent oxidation, 1H-pyrazin-2-ones were obtained. Transformation into the corresponding pyrazine triflates and substitution with primary or secondary amines led to 2-aminopyrazines. Since these syntheses take advantage of the readily available starting materials (e.g., amino acids, amino alcs., and amines) a variety of the entitled structures can be obtained in few, high yielding steps.

IT 786652-83-3P 786652-85-5P 786652-86-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of aminopyrazine via trifluoromethylsulfonylation of methyl(phenyl)pyrazinone followed by amination with amines)

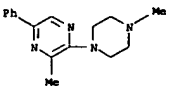
RN 786652-83-3 CAPLUS
CN Morpholine, 4-(3-methyl-5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



RN 786652-85-5 CAPLUS
CN 4-Piperidinemethanol, 1-(3-methyl-5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)



RN 786652-86-6 CAPLUS
CN Pyrazine, 3-methyl-2-(4-methyl-1-piperazinyl)-5-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

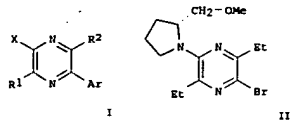
L10 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:453208 CAPLUS
DOCUMENT NUMBER: 141:23551
TITLE: Preparation of pyrrolidinylpyrazines as CRF-1 receptor modulators for the treatment of anxiety-related disorders.
INVENTOR(S): Mickelson, John Warren
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, LLC, USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

APPLICANTS

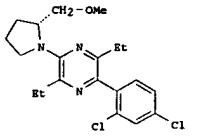
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004046136	A1	20040603	WO 2003-IB5183	20031111
WO 2004046136	C2	20050526		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2499133	AA	20040603	CA 2003-2499133	20031111
EP 1565454	A1	20050824	EP 2003-769841	20031111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015845	A	20050927	BR 2003-15845	20031111
US 2004157860	A1	20040812	US 2003-706555	20031112
PRIORITY APPLN. INFO.:			US 2002-428145P	P 20021121
			WO 2003-IB5183	W 20031111

OTHER SOURCE(S): MARPAT 141:23551
GI



I

II



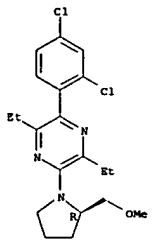
III

AB Title compds. I [X = (un)substituted monocyclic group, e.g., aryl cycloalkyl, heteroaryl cycloalkyl, aryl heterocycloalkyl, etc.; Ar = (un)substituted aryl, heteroaryl; R1, R2 = H, halo, NO2, etc.] and their pharmaceutically acceptable salts were prepared For example, palladium mediated coupling of bromopyrazine II, e.g., prepared from (R)-2-[methoxymethyl]pyrrolidine in 2-steps, and (2,4-dichlorophenyl)boronic acid afforded pyrrolidinylpyrazine III. In CRF-1 receptor binding assays, compds. I exhibited IC50 values generally ranging from 0.5 nM-10 μM (sic). Compds. I are useful for the treatment of anxiety or affective disorders.

IT 697767-72-9P 697767-74-1P 697767-76-3P
697767-78-5P 697767-79-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidinylpyrazines as CRF-1 receptor modulators for the treatment of anxiety-related disorders.)

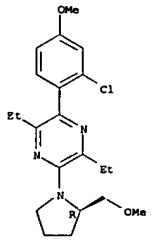
RN 697767-72-9 CAPLUS
CN Pyrazine, 2-(2,4-dichlorophenyl)-3,6-diethyl-5-[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



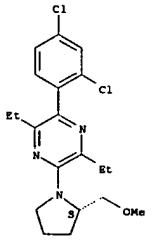
RN 697767-74-1 CAPLUS
CN Pyrazine, 2-(2-chloro-4-methoxyphenyl)-3,6-diethyl-5-[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



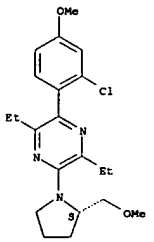
RN 697767-76-3 CAPLUS
CN Pyrazine, 2-(2,4-dichlorophenyl)-3,6-diethyl-5-[(2S)-2-(methoxymethyl)-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



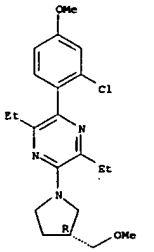
RN 697767-78-5 CAPLUS
CN Pyrazine, 2-(2-chloro-4-methoxyphenyl)-3,6-diethyl-5-[(2S)-2-(methoxymethyl)-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 697767-79-6 CAPLUS
CN Pyrazine, 2-(2-chloro-4-methoxyphenyl)-3,6-diethyl-5-[(3R)-3-(methoxymethyl)-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



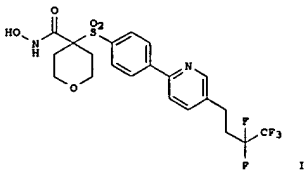
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:2857 CAPLUS
DOCUMENT NUMBER: 140:59663
TITLE: Preparation of arylsulfonylhydroxamic acid and amide derivatives as protease inhibitors
INVENTOR(S): Chen, Yiyuan; Freskos, John N.; Gasiecki, Alan F.; Grapperhaus, Margaret L.; Hansen, Donald W., Jr.; Heintz, Robert M.; Khanna, Ish K.; Kolodziej, Steve A.; Mantegani, Sergio; Masse, Mark A.; McDonald, Joseph J.; Mischke, Deborah A.; Nagy, Mark A.; Perrone, Ettore; Schmidt, Michelle A.; Spangler, Dale P.; Talley, John J.; Trivedi, Mahima; Wynn, Thomas A.; Becker, Daniel P.; Rico, Joseph G.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 443 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000811	A1	20031231	WO 2003-US20028	20030625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2490646	AA	20031231	CA 2003-2490646	20030625
US 2004167182	A1	20040826	US 2003-603441	20030625
EP 1515951	A1	20050323	EP 2003-742193	20030625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003012036	A	20050405	BR 2003-12036	20030625
PRIORITY APPLN. INFO.:			US 2002-391329P	P 20020625
			WO 2003-US20028	W 20030625

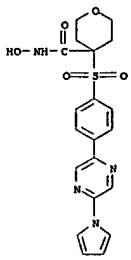
OTHER SOURCE(S): MARPAT 140:59663
GI



AB This invention is directed generally to hydroxamic acid and amide compds. (including salts of such compds.), and, more particularly, to aryl- and heteroaryl- arylsulfonylmethyl hydroxamic acids and amides that, inter alia, inhibit protease activity, particularly matrix metalloproteinase (also known as "matrix metalloprotease" or "MMP") activity and/or aggrecanase activity. These compds. generally correspond in structure to formula A1NHC(O)C(A2)(A3)SO2E1E2E3E4 [A1 = H, OH, carbocyclyloxy, heterocyclyloxy; A2 and A3, together with the carbon atom to which they are bonded, form (un)substituted heterocyclyl or carbocyclyl; or A2, A3 = H, alkyl, alkoxyalkyl, etc.; E1 = (un)substituted aryl; E2 = (un)substituted (hetero)aryl; E3 = O, CO, CO2, OCO, NH, S, etc.; E4 = alkyl, alkenyl, alkoxyalkyl, etc.]. E.g., a multi-step synthesis of I.HCl which showed Ki of 4723 nM, 0.0708 nM, 0.258 nM, 0.0403 nM and 523 nM against MMP-1, MMP-2, MMP-9, MMP-13 and MMP-14, resp., was given. This invention also is directed to compns. of such compds., intermediates for the syntheses of such compds., methods for making such compds., and methods for treating conditions associated with MMP activity and/or aggrecanase activity, particularly pathol. conditions.

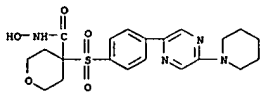
IT 639493-88-2P 639495-02-6P 639495-25-3P
639498-40-1P 639498-41-2P 639498-42-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylsulfonylhydroxamic acid and amide derivs. as protease inhibitors)

RN 639493-88-2 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(1H-pyrrol-1-yl)pyrazinyl]phenyl]sulfonyl]-, dihydrochloride (9CI) (CA INDEX NAME)



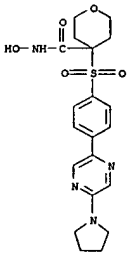
●2 HCl

RN 639495-02-6 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(1-piperidinyl)pyrazinyl]phenyl]sulfonyl]-, dihydrochloride (9CI) (CA INDEX NAME)



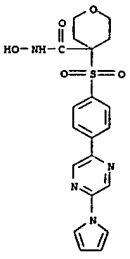
●2 HCl

RN 639495-25-3 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(1-pyrrolidinyl)pyrazinyl]phenyl]sulfonyl]-, dihydrochloride (9CI) (CA INDEX NAME)

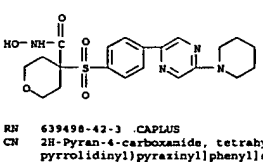


●2 HCl

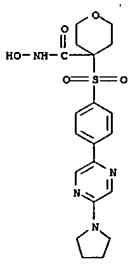
RN 639498-40-1 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(1H-pyrrol-1-yl)pyrazinyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 639498-41-2 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(1-piperidinyl)pyrazinyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 639498-42-3 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(1-pyrrolidinyl)pyrazinyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

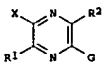


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:875261 CAPLUS
DOCUMENT NUMBER: 139:381508
TITLE: Preparation of pyrazines as CRF1 receptor antagonists.
INVENTOR(S): Corbett, Jeffrey W.; Ennis, Michael D.; Frank, Kristine E.; Fu, Jian-Min; Hoffman, Robert L.; Verhoest, Patrick R.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091225	A1	20031106	WO 2003-US10474	20030417
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2480497	AA	20031106	CA 2003-2480497	20030417
US 2004053941	A1	20040318	US 2003-417867	20030417
EP 1499599	A1	20050126	EP 2003-719605	20030417
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009551	A	20050209	BR 2003-9551	20030417
JP 2005533014	T2	20051104	JP 2003-587785	20030417
PRIORITY APPLN. INFO.:			US 2002-376031P	P 20020426
			WO 2003-US10474	W 20030417

OTHER SOURCE(S): MARPAT 139:381508
GI

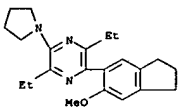


I

AB Title compds. [I; R1, R2 = halo, NO2, CN, Ra, ORa, SOmRa, NRaRa, CONRaRa, CSNRaRa, SOmNRaRa, NRaSOmRa, NRaCO2Ra, NRaC(S)ORa, O2CNRaRa, OC(S)NRaRa, NRaCONRaRa, NRaCSNRaRa, CO2Ra, C(S)ORa, O2CORa, CRaRaAr; X = NR3R4, OR3, CR3R4R5, COR3, CSR3, SOmR3, NR3COR4, NR3CSR4, NR3SOmR4, R3; R3-R5 = Ra, substituted A, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, arylcycloalkyl, heteroarylcycloalkyl, arylheterocycloalkyl, heteroarylheterocycloalkyl; Ra = H, A, cycloalkyl, haloalkyl, aryl, heteroaryl, heterocycloalkyl, where Ra may be substituted with 1-5 of Rt, ORt, SOmRt, NRtRt, O, S; Rt = H, halo, NO2, NH2, OH, SH, CN, CONH2, CSNH2, CONHA, CSNHA, CONA2, CSNA2, OA, NHA, NA2, SOmA, SO2NH2, SO2NHA, SO2NA2, A, cycloalkyl, haloalkyl, Ph, PhCH2, heteroaryl, heterocycloalkyl where Ph, PhCH2, heteroaryl, heterocycloalkyl may be substituted with A, halo; G = O1, O2 (substituted) by halo, CN, NO2, O, S, OR5, SR5, NR5R5, COR5, C(S)R5, CO2R5, C(S)OR5, CONR5R5, CSNR5R5, SOmR5, SO2NR5R5, NR5COR5, NR5CSR5, NR5CO2R5, NR5C(S)OR5, NR5CONR5R55, NR5CSNR5R55, NR5SO2R5, O2CR5, OC(S)R5, OC(O)OR5, OC(S)OR5, O2CNR5R5, OC(S)NR5R55, CR5R5Ar, (substituted) A, cycloalkyl, aryl, heteroaryl, heterocycloalkyl; G groups may contain ≤1 double bond in its nonarom. ring; Ar = (substituted) aryl, heteroaryl; A = alkyl; m, n = 0-2], were prepared as CRF1 receptor antagonists (no data). Thus, 5-bromo-3,6-diethyl-N-(1-ethylpropyl)pyrazin-2-amine (preparation given), 6-methoxy-2,3-dihydro-1H-inden-5-ylboronic acid (preparation given), tetrakis(triphenylphosphine)palladium(0), 2M Na2CO3, and ethylene glycol di-Me ether were heated together on an orbital shaker at 80° for 30 h to give 66% 3,6-diethyl-N-(1-ethylpropyl)-5-(6-methoxy-2,3-dihydro-1H-inden-5-yl)pyrazin-2-amine.

IT 622834-43-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of pyrazines as CRF1 receptor antagonists)

RN 622834-43-9 CAPLUS
CN Pyrazine, 2-(2,3-dihydro-6-methoxy-1H-inden-5-yl)-3,6-diethyl-5-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:133348 CAPLUS
DOCUMENT NUMBER: 138:187790
TITLE: Preparation of arylpiperazines and arylpiperidines as metalloproteinase inhibitors
INVENTOR(S): Finlay, Raymond; Waterson, David
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014092	A1	20030220	WO 2002-SE1437	20020808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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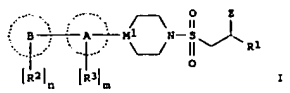
EP 1417181	A1	20040512	EP 2002-756052	20020808
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005501087	T2	20050113	JP 2003-519042	20020808
US 2004180901	A1	20040916	US 2004-485675	20040129
PRIORITY APPLN. INFO.:			GB 2001-19472 A	20010809
			WO 2002-SE1437 W	20020808

OTHER SOURCE(S): MARPAT 138:187790
GI



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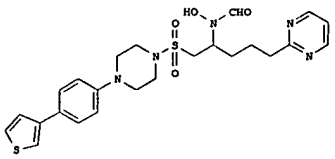
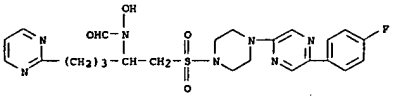


II

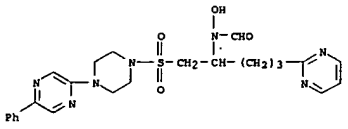
AB The title compds. I [A, B = Ph, heteroaryl; at least one of A and B = heteroaryl; n, m = 0-3; R2, R3 = OH, NO2, CF3, etc.; M1 = N, C; R1 = XY; X = alkylene; Y = (un)substituted cycloalkyl, aryl, heteroaryl; Z = N(OH)CHO, CONHOH], useful as metalloproteinase inhibitors, especially as inhibitors of MMP 13, were prepared E.g., a 5-step synthesis of II, starting from 1-(4-bromophenyl)piperazine.HCl, was given.

IT 497922-53-9P 497922-56-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylpiperazines and arylpiperidines as metalloproteinase inhibitors)

RN 497922-53-9 CAPLUS
CN Piperazine, 1-[5-(4-fluorophenyl)pyrazinyl]-4-[[2-(formylhydroxyamino)-5-(2-pyrimidinyl)pentyl]sulfonyl]- (9CI) (CA INDEX NAME)

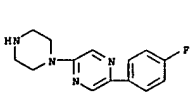


RN 497922-56-2 CAPLUS
CN Piperazine, 1-[[2-(formylhydroxyamino)-5-(2-pyrimidinyl)pentyl]sulfonyl]-4-(5-phenylpyrazinyl)- (9CI) (CA INDEX NAME)

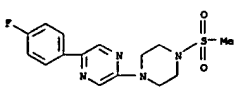


IT 497923-60-1P 497923-61-2P 497923-62-3P 497923-63-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of arylpiperazines and arylpiperidines as metalloproteinase inhibitors)

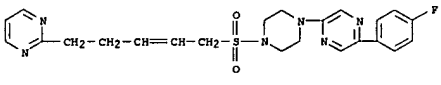
RN 497923-60-1 CAPLUS
CN Pyrazine, 2-(4-fluorophenyl)-5-(1-piperazinyl)- (9CI) (CA INDEX NAME)



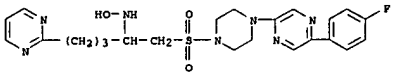
RN 497923-61-2 CAPLUS
CN Piperazine, 1-[5-(4-fluorophenyl)pyrazinyl]-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



RN 497923-62-3 CAPLUS
CN Piperazine, 1-[5-(4-fluorophenyl)pyrazinyl]-4-[[5-(2-pyrimidinyl)-2-pentenyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 497923-63-4 CAPLUS
CN Piperazine, 1-[5-(4-fluorophenyl)pyrazinyl]-4-[[2-(hydroxyamino)-5-(2-pyrimidinyl)pentyl]sulfonyl]- (9CI) (CA INDEX NAME)



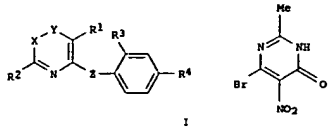
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:946274 CAPLUS
DOCUMENT NUMBER: 138:24735
TITLE: Preparation of pyrimidines, triazines and pyrazines as metabotropic glutamate receptor (mGluR1a) antagonists for the treatment of neurological disorders
INVENTOR(S): Binggeli, Alfred; Maerki, Hans-Peter; Masquelin, Thierry; Mutel, Vincent; Wilhelm, Maurice; Woestl, Wolfgang
PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098864	A1	20021212	WO 2002-EP5788	20020527
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2448602	AA	20021212	CA 2002-2448602	20020527
EP 1397351	A1	20040317	EP 2002-748720	20020527
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002010102	A	20040608	BR 2002-10102	20020527
CN 1512988	A	20040714	CN 2002-810987	20020527
JP 2004536814	T2	20041209	JP 2003-501988	20020527
US 2003060466	A1	20030327	US 2002-157338	20020529
US 6673795	B2	20040106		
ZA 2003008859	A	20050214	ZA 2003-8859	20031113

PRIORITY APPLN. INFO.: EP 2001-113379 A 20010601
WO 2002-EP5788 W 20020527

OTHER SOURCE(S): MARPAT 138:24735
GI



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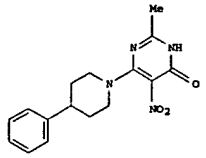
II

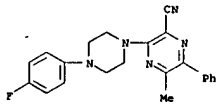


III

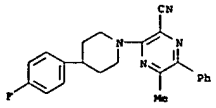
AB Title compds. I [R1 = NO2, CN; R2 = H, alkyl, NHR10; R10 = H, alkyl, -(CH2)mOR11, etc; R11 = H, alkyl; m = 2-6; R3 = H, alkyl, F, etc.; R4 = H, F; X-Y = N:N, N(R5)CO, N:CR6, etc.; R5 = H, alkyl, alkenyl, etc.; R6 = alkyl, H, halo, etc.] and their pharmaceutically acceptable salts were prepared For example, coupling of bromide II and 4-phenylpiperidine afforded pyrimidinone III. In mGluR1a receptor binding assays, 29-specific examples of compds. I exhibited IC50 values ranging from 1.8-0.017 μM, e.g., pyrimidinone III IC50 = 0.063 μM.

IT 478179-94-1P, 4-(4-Fluorophenyl)-6'-methyl-5'-phenyl-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl-3'-carbonitrile 478179-96-3P, 3-[4-(4-Fluorophenyl)piperidin-1-yl]-5-methyl-6-phenylpyrazine-2-carbonitrile
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidines, triazines and pyrazines as mGluR1a antagonists for the treatment of neurol. disorders)

RN 478179-94-1 CAPLUS
CN Pyrazinecarbonitrile, 3-[4-(4-fluorophenyl)-1-piperazinyl]-5-methyl-6-phenyl- (9CI) (CA INDEX NAME)



RN 478179-96-3 CAPLUS
CN Pyrazinecarbonitrile, 3-[4-(4-fluorophenyl)-1-piperidinyl]-5-methyl-6-phenyl- (9CI) (CA INDEX NAME)

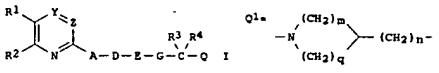


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:849591 CAPLUS
DOCUMENT NUMBER: 137:370112
TITLE: Preparation of derivatives of heterocyclic compounds such as pyridine, pyrimidine, 1,2,4-triazine, and pyrazine as antagonists of prostaglandin I2 receptor
INVENTOR(S): Asaki, Tetsuo; Hamamoto, Taisuke; Kuwano, Keiichi
PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088084	A1	20021107	WO 2002-JP4118	20020425
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2445344	AA	20021107	CA 2002-2445344	20020425
EP 1400518	A1	20040324	EP 2002-722772	20020425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002009249	A	20040608	BR 2002-9249	20020425
CN 1516690	A	20040728	CN 2002-808977	20020425
US 2004102436	A1	20040527	US 2003-476196	20031023
PRIORITY APPLN. INFO.:			JP 2001-129765 A	20010426
			WO 2002-JP4118 W	20020425

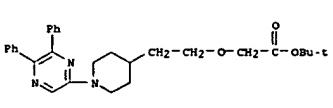
OTHER SOURCE(S): MARPAT 137:370112
GI



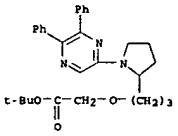
AB The invention provides compds. useful as PGI2 receptor agonist and pharmaceutical compns., particularly pharmaceutical compns. containing as the active ingredient compds. represented by the general formula (I) or pharmaceutically acceptable salts thereof [wherein R1 and R2 are each independently optionally substituted aryl; Y is N, N(O), or optionally substituted CH; Z is N or optionally substituted CH; A is optionally substituted NH, O, S, SO, SO2, or ethylene; D is an optionally hydroxy-substituted alkylene or alkenylene; or A and D together represent a bivalent group Q1 (wherein m is an integer of 0-2; q is 2 or 3; n is an integer of 0-4); E is phenylene or a single bond; G is O, S, or optionally substituted CH2; R3 and R4 are each independently hydrogen or alkyl; and Q is carboxyl, alkoxycarbonyl, tetrazolyl, carbamoyl, mono- or dialkylcarbamoyl, CONHSO2R10 (wherein R10 is optionally substituted alkyl, aryl, aryloxy, or heterocyclyl)]. These compds. are useful as platelet aggregation inhibitors or remedies for chronic artery obstruction, intermittent limping (claudication) (Charcot's syndrome), or peripheral artery embolism. Thus, a solution of 763 mg 5,6-diphenyl-2-(methylamino)pyrazine in 4 mL DMF was added 140 mg 60% NaH, stirred at 80° for 30 min, and cooled in an ice bath followed by adding slowly a solution of 657 mg Me 2-(4-bromobutyloxy)acetate in 2 mL DMF, and the resulting mixture was stirred at room temperature for 14 h to give 240 mg Me 2-[4-[N-(5,6-diphenylpyrazin-2-yl)-N-methylamino]butyloxy]acetate (II). II was saponified with a mixture of 1 N aqueous NaOH and MeOH under reflux for 2 h, followed by removing the solvent under reduced pressure, adding water, extracting the aqueous solution with Et2O, neutralizing it with 1 N aqueous HCl, and extracting it with EtOAc to give 2-[4-[N-(5,6-diphenylpyrazin-2-yl)-N-methylamino]butyloxy]acetic acid (III). III showed IC50 of 0.2 μM for inhibiting the ADP (ADT)-induced aggregation of human blood platelet and at 1 μM inhibited the [3H]-Iloprost binding on human platelet membrane by 85%. Pharmaceutical formulations, e.g. tablet containing tert-Bu 2-[4-(5,6-diphenylpyrazin-2-ylsulfonyl)butyloxy]acetate, were described.

IT 475085-08-6P 475085-09-7P 475085-11-1P 475085-12-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of derivs. of heterocyclic compds. as antagonists of prostaglandin I2 receptor platelet aggregation inhibitor, or remedy for chronic artery obstruction, intermittent limping, or peripheral artery embolism)

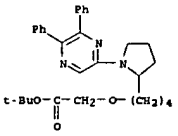
RN 475085-08-6 CAPLUS
CN Acetic acid, [2-[1-(5,6-diphenylpyrazinyl)-4-piperidinyl]ethoxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



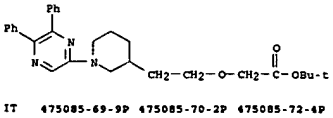
RN 475085-09-7 CAPLUS
CN Acetic acid, [3-[1-(5,6-diphenylpyrazinyl)-2-pyrrolidinyl]propoxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 475085-11-1 CAPLUS
CN Acetic acid, [4-[1-(5,6-diphenylpyrazinyl)-2-pyrrolidinyl]butoxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

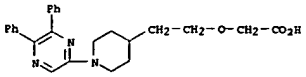


RN 475085-12-2 CAPLUS
CN Acetic acid, [2-[1-(5,6-diphenylpyrazinyl)-3-piperidinyl]ethoxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

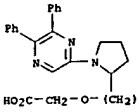


IT 475085-69-9P 475085-70-2P 475085-72-4P 475085-73-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of derivs. of heterocyclic compds. as antagonists of prostaglandin I2 receptor platelet aggregation inhibitor, or remedy for chronic artery obstruction, intermittent limping, or peripheral artery embolism)

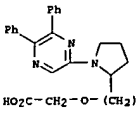
RN 475085-69-9 CAPLUS
CN Acetic acid, [2-[1-(5,6-diphenylpyrazinyl)-4-piperidinyl]ethoxy]- (9CI) (CA INDEX NAME)



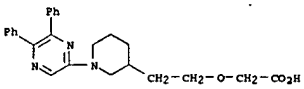
RN 475085-70-2 CAPLUS
CN Acetic acid, [3-[1-(5,6-diphenylpyrazinyl)-2-pyrrolidinyl]propoxy]- (9CI) (CA INDEX NAME)



RN 475085-72-4 CAPLUS
CN Acetic acid, [4-[1-(5,6-diphenylpyrazinyl)-2-pyrrolidinyl]butoxy]- (9CI) (CA INDEX NAME)

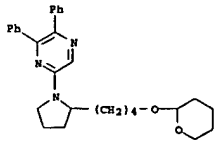


RN 475085-73-5 CAPLUS
CN Acetic acid, [2-[1-(5,6-diphenylpyrazinyl)-3-piperidinyl]ethoxy]- (9CI) (CA INDEX NAME)

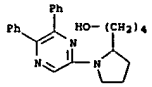


IT 475086-78-3P 475086-79-4P 475086-80-7P
475086-81-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of derive. of heterocyclic compds. as antagonists of prostaglandin I2 receptor platelet aggregation inhibitor, or remedy for chronic artery obstruction, intermittent limping, or peripheral artery embolism)

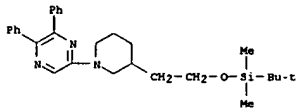
RN 475086-78-3 CAPLUS
CN Pyrazine, 2,3-diphenyl-5-[2-[4-[(tetrahydro-2H-pyran-2-yl)oxy]butyl]-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)



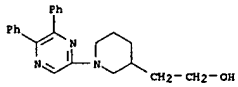
RN 475086-79-4 CAPLUS
CN 2-Pyrrolidinebutanol, 1-(5,6-diphenylpyrazinyl)- (9CI) (CA INDEX NAME)



RN 475086-80-7 CAPLUS
CN Pyrazine, 5-[3-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethyl]-1-piperidinyl]-2,3-diphenyl- (9CI) (CA INDEX NAME)



RN 475086-81-8 CAPLUS
CN 3-Piperidineethanol, 1-(5,6-diphenylpyrazinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

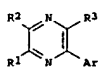
L10 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:617986 CAPLUS
DOCUMENT NUMBER: 135:180787
TITLE: Preparation of substituted arylpyrazines and their binding with CRF1 receptors
INVENTOR(S): Yoon, Taeyoung; Ge, Ping; Horvath, Raymond F.; De Lombaert, Stephane; Hodgetts, Kevin J.; Doller, Dario; Zhang, Cunyu
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 193 pp.

102(e)

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060806	A2	20010823	WO 2001-US5264	20010216
WO 2001060806	A3	20020207		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2398937	AA	20010823	CA 2001-2398937	20010216
EP 1255740	A2	20021113	EP 2001-910939	20010216
EP 1255740	B1	20051019		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003018035	A1	20030123	US 2001-788315	20010216
EE 200200453	A	20031215	EE 2002-453	20010216
JP 2004500383	T2	20040108	JP 2001-560191	20010216
BR 2001008363	A	20040210	BR 2001-8363	20010216
EP 1500653	A1	20050126	EP 2004-25531	20010216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 520484	A	20050324	NZ 2001-520484	20010216
BG 106968	A	20030430	BG 2002-106968	20020731
ZA 2002006103	A	20030820	ZA 2002-6103	20020731
NO 2002003869	A	20020911	NO 2002-3869	20020815
US 2005215559	A1	20050929	US 2005-107148	20050415
PRIORITY APPLN. INFO.:			US 2000-182934P	P 20000216
			US 2000-206455P	P 20000522
			EP 2001-910939	A3 20010216
			US 2001-788315	A3 20010216
			WO 2001-US5264	W 20010216

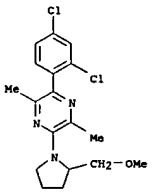
OTHER SOURCE(S): MARPAT 135:180787
GI



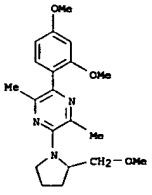
AB Arylpyrazine compds. I [Ar = substituted Ph, naphthyl, heterocyclyl; R1, R3 = H, halo, cyano, NO2, etc.; R2 = halo, amino, alkyl, etc.], including arylpyrazines that can bind with high affinity and high selectivity to CRF1 receptors, including human CRF1 receptors, were prepared E.g., N-(1-ethylpropyl)-5-(2,4-dimethoxyphenyl)-3,6-dimethylpyrazine-2-amine was prepared by reaction of 2-chloro-3,6-dimethylpyrazine with 1-ethylpropylamine, followed by bromination and reaction with 2,4-dimethoxybenzeneboronic acid.

IT 355834-42-3P 355834-43-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted arylpyrazines and their binding with CRF1 receptors)

RN 355834-42-3 CAPLUS
CN Pyrazine, 2-(2,4-dichlorophenyl)-5-[2-(methoxymethyl)-1-pyrrolidinyl]-3,6-dimethyl- (9CI) (CA INDEX NAME)



RN 355834-43-4 CAPLUS
CN Pyrazine, 2-(2,4-dimethoxyphenyl)-5-[2-(methoxymethyl)-1-pyrrolidinyl]-3,6-dimethyl- (9CI) (CA INDEX NAME)



L10 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:608606 CAPLUS
DOCUMENT NUMBER: 129:230741
TITLE: Preparation of pyrazines as anticonvulsants
INVENTOR(S): Cox, Brian; Nobbs, Malcolm Stuart; Shah, Gita Punjabhai; Edney, Dean David; Loft, Michael Simon
PATENT ASSIGNEE(S): Glaxo Group Ltd., UK
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9838174	A1	19980903	WO 1998-EP1077	19980216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,				

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2282585	AA	19980903	CA 1998-2282585	19980226
AU 9868237	A1	19980918	AU 1998-68237	19980226
AU 732915	B2	20010503		
ZA 9801624	A	19990826	ZA 1998-1624	19980226
EP 966448	A1	19991229	EP 1998-913592	19980226
EP 966448	B1	20031001		

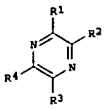
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

BR 9807814	A	20000222	BR 1998-7814	19980226
EE 9900376	A	20000417	EE 1999-376	19980226
TR 9902082	T2	20000421	TR 1999-9902082	19980226
JP 2000511203	T2	20000829	JP 1998-537310	19980226
JP 3369189	B2	20030120		
NZ 337121	A	20010330	NZ 1998-337121	19980226
JP 2002308773	A2	20021023	JP 2002-47974	19980226
CN 1105111	B	20030409	CN 1998-804593	19980226
IL 131293	A1	20030731	IL 1998-131293	19980226
AT 251143	E	20031015	AT 1998-913592	19980226
PT 966448	T	20040227	PT 1998-913592	19980226
ES 2205469	T3	20040501	ES 1998-913592	19980226
CZ 295618	B6	20050914	CZ 1999-3111	19980226
TW 513416	B	20021211	TW 1998-87103079	19980303
US 6255307	B1	20010703	US 1999-380062	19990825
MX 9907910	A	20000228	MX 1999-7910	19990826
NO 9904213	A	19991029	NO 1999-4213	19990831
NO 313363	B1	20020923		
BG 103723	A	20010531	BG 1999-103723	19990909
HK 1023116	A1	20040116	HK 2000-102173	20000410
US 2002169172	A1	20021114	US 2001-855703	20010516
US 6599905	B2	20030729		

PRIORITY APPLN. INFO.:		GB 1997-4275	A 19970301
		GB 1997-8183	A 19970423
		JP 1998-537310	A3 19980226
		WO 1998-EP1077	W 19980226
		US 1999-380062	A3 19990825

OTHER SOURCE(S): MARPAT 129:230741

GI



I

AB The title compds. {I; R1 (un)substituted by one or more halo atoms Ph, naphthyl; R2 = NH2, NHC(O)Ra; R3 = NRbRc, NHC(O)Ra, H; R4 = H, (un)substituted by one or more halo atoms C1-4 alkyl, CN, etc.; Ra = C1-4 alkyl, C3-7 cycloalkyl; Rb, Rc = H, C1-4 alkyl; NRbRc = (un)substituted 6-membered nitrogen containing heterocycle; with the proviso that R1 does not represent 4-ClC6H4 when R2 = NH2, and R3, R4 = H}, useful in the treatment of epilepsy, bipolar disorder or manic depression, pain, functional bowel disorders, neurodegenerative diseases, neuroprotection, neurodegeneration, or prevention or reducing dependence on, or preventing or reducing tolerance or reverse tolerance to, a dependence-inducing agent, were prepared and formulated. Thus, treatment of 2-amino-6-chloro-3-(2,3,5-trichlorophenyl)pyrazine (preparation described) with aqueous ammonia in EtOH afforded 56% I [R1 = 2,3,5-Cl3C6H2; R2 = R3 = NH2; R4 = H]. Compds. I exhibited ED50's of 1-20 mg/kg when tested for antiepileptic activity.

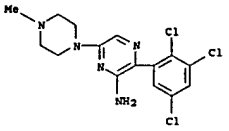
IT 212778-94-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrazines as anticonvulsants)

RN 212778-94-4 CAPLUS

CN Pyrazinamine, 6-(4-methyl-1-piperazinyl)-3-(2,3,5-trichlorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:551083 CAPLUS

DOCUMENT NUMBER: 125:181512

TITLE: Optically active compound, liquid crystal composition containing the same and liquid crystal device

INVENTOR(S): Takiguchi, Takao; Iwaki, Takashi; Tokano, Goji; Kosaka, Yoko; Nakamura, Shinichi

PATENT ASSIGNEE(S): Canon Kk, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 39 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08151577	A2	19960611	JP 1994-319499	19941130

PRIORITY APPLN. INFO.: JP 1994-319499 19941130

OTHER SOURCE(S): MARPAT 125:181512

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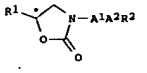


I

AB The title compound is represented by I (R1, R2 = C2-20 alkyl; A1 = pyrimidine-2,5-diyl, pyridine-2,5-diyl, etc.; A2 = A1, single bond, 1,4-phenylene, 1,4-cyclohexylene, 1,3-dioxane-2,5-diyl, 1,3-dithiane-2,5-diyl). The composition contains 1-80 % of the compound The composition shows a chiral smectic phase. The device showed improved switching characteristics suitable for liquid crystal displays and liquid crystal shutters.

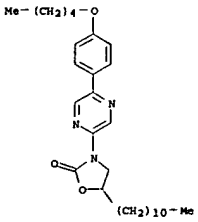
IT 180845-17-4

RL: DEV (Device component use); USES (Uses)

(optically active compound for liquid crystal composition of liquid crystal display)

RN 180845-17-4 CAPLUS

CN 2-Oxazolidinone, 3-[5-[4-(pentyloxy)phenyl]pyrazinyl]-5-undecyl- (9CI) (CA INDEX NAME)



L10 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:234009 CAPLUS

DOCUMENT NUMBER: 118:234009

TITLE: Studies on as-triazine derivatives. XIX. Synthesis of 2,3-diarylpyrazine and 2,3-diarylpyridine derivatives as blood platelet aggregation inhibitors

AUTHOR(S): Konno, Shoetsu; Matsuya, Yuji; Kumazawa, Minako; Amano, Masaki; Kokubo, Takeshi; Sagi, Mataichi; Yamanaka, Hiroshi

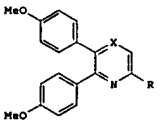
CORPORATE SOURCE: Pharm. Inst., Tohoku Univ., Sendai, 980, Japan

SOURCE: Yakugaku Zasshi (1993), 113(1), 40-52
CODEN: YKKZAJ; ISSN: 0031-6903

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

GI



I

AB 4,5-Diphenyl-2-ethoxypyrimidine, 3,4-diphenyl-6-ethoxypyridazine, and 2,3-diphenyl-5-ethoxypyrazine were evaluated for inhibitory activity towards arachidonic acid-induced aggregation of rabbit blood platelet in vitro. 2,3-Diphenyl-5-ethoxypyrazine exhibited significant inhibitory activity. Various 5-substituted 2,3-bis(4-methoxyphenyl)pyrazines I (X = N R = OMe, OEt OPr, OBu, OC5H11-n, OCHMe2, OCH2CHMe2, OCH2R1, SEt, SMe, NHEt, piperidino, N-methylpiperazino, R1 = cyclopropyl) were synthesized by the nucleophilic substitution reaction of 5-chloro-2,3-bis(4-methoxyphenyl)pyrazine. In a similar manner, substituted 2,3-bis(4-methoxyphenylpyridines I (X = CH, R as above) were prepared from 2,3-bis(4-methoxyphenyl)-6-methylsulfonylpyridine, which was synthesized by the cycloaddn.-retro Diels-Alder reaction of 5,6-bis(4-methoxyphenyl)-3-methylsulfonyl-1,2,4-triazine with norbornadiene. Among the compds. prepared, I (X = N, R = OCHMe2) showed the most potent inhibitory activity, which was more than the activity of anitrazafen.

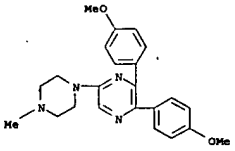
IT 141425-23-2P 147593-65-5P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and blood platelet aggregation inhibition by)

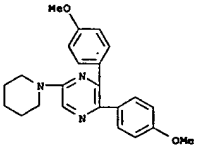
RN 141425-23-2 CAPLUS

CN Pyrazine, 2,3-bis(4-methoxyphenyl)-5-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



RN 147593-65-5 CAPLUS

CN Pyrazine, 2,3-bis(4-methoxyphenyl)-5-(1-piperidinyl)- (9CI) (CA INDEX NAME)



L10 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:235661 CAPLUS

DOCUMENT NUMBER: 116:235661

TITLE: Preparation of diphenylazines as antithrombotics vasodilators, antihypertensives, and antiinflammatories

INVENTOR(S): Takasugi, Hisashi; Sakai, Hiroyoshi; Tanaka, Akito; Ishikawa, Takatoshi

PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

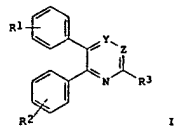
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9202513	A1	19920220	WO 1991-JP1042		19910805
W: JP, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE					
JP 06501926	T2	19940303	JP 1991-513247		19910805
PRIORITY APPLN. INFO.:			GB 1990-17183	A	19900806
			GB 1990-20345	A	19900918
			WO 1991-JP1042	W	19910805

OTHER SOURCE(S): MARPAT 116:235661
GI



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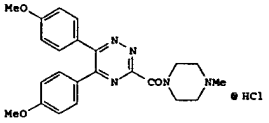
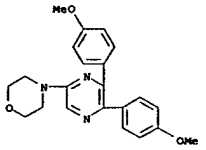


II

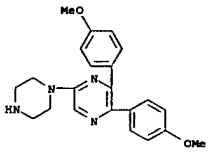
AB Title compds. [I; R1,R2 = alkoxy; R3 = (substituted) (tetrahydro)pyridyl, piperidyl, piperazinyl, morpholinyl, substituted amino, carboxyalkyl, carboxyalkenyl, hydroxyalkyl, CHO, EtO2C, alkylaminocarbonyl, etc.; Y,Z = CH, N], were prepared Thus, 3-ethoxycarbonyl-5,6-bis(4-methoxyphenyl)-1,2,4-triazine and N-methylpiperazine were heated at 80-90° for 4 h 40 min to give, after treatment with HCl in EtOH, title compound II. In an ex vivo screen, II at 1.0 mg/kg orally gave 100% inhibition of arachidonic acid induced platelet aggregation in guinea pig platelet rich plasma.

IT 141425-21-0P 141425-22-1P 141425-23-2P
141425-24-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as cardiovascular agent)

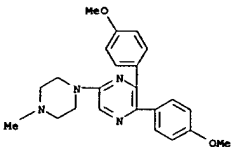
RN 141425-21-0 CAPLUS
CN Morpholine, 4-[5,6-bis(4-methoxyphenyl)pyrazinyl]- (9CI) (CA INDEX NAME)



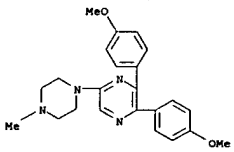
RN 141425-22-1 CAPLUS
CN Pyrazine, 2,3-bis(4-methoxyphenyl)-5-(1-piperazinyl)- (9CI) (CA INDEX NAME)



RN 141425-23-2 CAPLUS
CN Pyrazine, 2,3-bis(4-methoxyphenyl)-5-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



RN 141425-24-3 CAPLUS
CN Pyrazine, 2,3-bis(4-methoxyphenyl)-5-(4-methyl-1-piperazinyl)-, dihydrochloride (9CI) (CA INDEX NAME)

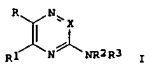


●2 HCl

L10 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:103396 CAPLUS
DOCUMENT NUMBER: 100:103396
TITLE: 1,2,4-Triazine and pyrazine derivatives
INVENTOR(S): Wong, David Taiwai; Lacefield, William Bryant
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 48 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 88593	A2	19830914	EP 1983-301142		19830303
EP 88593	A3	19840523			
EP 88593	B1	19870527			
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
US 4513135	A	19850423	US 1982-354982		19820305
DK 8300972	A	19830906	DK 1983-972		19830228
RO 86320	B3	19850315	RO 1983-110181		19830228
IL 68002	A1	19860930	IL 1983-68002		19830228
ZA 8301387	A	19841031	ZA 1983-1387		19830301
FI 8300708	A	19830906	FI 1983-708		19830302
JP 58162582	A2	19830927	JP 1983-35221		19830302
AU 8312029	A1	19830908	AU 1983-12029		19830303
AU 547581	B2	19851024			
GB 2116179	A1	19830921	GB 1983-5846		19830303
GB 2116179	B2	19850911			
CA 1195327	A1	19851015	CA 1983-422805		19830303
AT 27457	E	19870615	AT 1983-301142		19830303
DD 207716	A5	19840314	DD 1983-248497		19830304
ES 520340	A1	19840416	ES 1983-520340		19830304
HU 31175	O	19840428	HU 1983-762		19830304
HU 191368	B	19870227			
ES 526297	A1	19850416	ES 1983-526297		19831006
US 4585861	A	19860429	US 1985-688946		19850104
PRIORITY APPLN. INFO.:			US 1982-354982	A	19820305
			EP 1983-301142	A	19830303

OTHER SOURCE(S): CASREACT 100:103396
GI

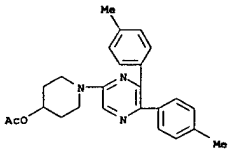


I

AB The title compds. I (X = CH, N; R,R1 = substituted Ph; NR2R3 = heterocyclic amino) were prepared Thus 3-methylthio-5,6-bis(4-methylphenyl)triazine was prepared by methylating the mercaptan and was treated with 4-piperidinol to give I (R = R1 = 4-MeC6H4, NR2R3 = 4-hydroxypiperidino, X = N) which at 900 nM gave a 50% increase in GABA binding in vitro.

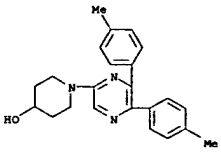
IT 88300-51-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and GABA binding activity of)

RN 88300-51-0 CAPLUS
CN 4-Piperidinol, 1-[5,6-bis(4-methylphenyl)pyrazinyl]-, acetate (ester) (9CI) (CA INDEX NAME)



IT 88300-50-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, acylation, and GABA binding activity of)

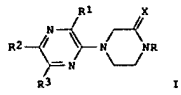
RN 88300-50-9 CAPLUS
CN 4-Piperidinol, 1-[5,6-bis(4-methylphenyl)pyrazinyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:400327 CAPLUS
DOCUMENT NUMBER: 89:327
TITLE: Piperazinylpyrazines with central serotoninmimetic activity
AUTHOR(S): Lumma, William C., Jr.; Hartman, Richard D.; Saari,

Walfred S.; Engelhardt, Edward L.; Hirschmann, Ralph; Clineschmidt, Bradley V.; Torchiana, Mary Lou; Stone, Clement A.

CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab., West Point, PA, USA
SOURCE: Journal of Medicinal Chemistry (1978), 21(6), 536-42
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

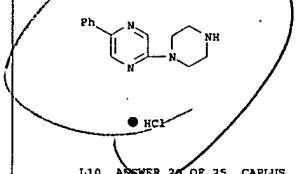


I

102(b)

AB Twenty title compds. I [R = H, (CH2)3NMe2, or 6-chloro-2-pyrazinyl; R = H or Cl; R2 = H, Cl, Ph, or CO2Me; R3 = H, Cl, Me, SPh, etc.; X = 2H or O] were synthesized by reaction of the appropriate chloropyrazine with piperazine [110-85-0] or an N-substituted piperazine. I; (R = R1 = R2 = H; R3 = Cl; X = 2H,.HCl) [61655-58-1] had pharmacol. properties in mice characteristic of potent central serotoninmimetic activity and only weak peripheral serotoninmimetic action in isolated rat uterus. Preferred conformations of this compound, determined by classical strain energy calcns. and CNDO mol. orbital techniques, were compared with serotonin [50-67-9] in order to determination those structural features which might interact with serotonin receptors.

IT 61655-63-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and serotoninmimetic activity of)
RN 61655-63-8 CAPLUS
CN Pyrazine, 2-phenyl-5-(1-piperazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



L10 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1977:72702 CAPLUS
DOCUMENT NUMBER: 86:72702
TITLE: Anorectic substituted (1'-piperazinyl)pyrazine derivatives
INVENTOR(S): Saari, Walfred S.; Lumma, William C., Jr.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Ger. Offen., 37 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2

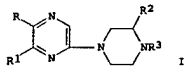
102(b)

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2617205	A1	19761028	DE 1976-2617205	19760420
DE 2617205	B2	19800508		
DE 2617205	C3	19810129		
DK 7601644	A	19761022	DK 1976-1644	19760407
DK 143899	B	19811026		
DK 143899	C	19820413		
SE 7604093	A	19761022	SE 1976-4093	19760407
SE 421695	B	19820125		
SE 421695	C	19820506		
NO 7601207	A	19761022	NO 1976-1207	19760408
NO 146599	B	19820726		
NO 146599	C	19821103		
FI 7600978	A	19761022	FI 1976-978	19760409
FI 62666	B	19821029		
FI 62666	C	19830210		
NL 7603800	A	19761025	NL 1976-3800	19760409
NL 167692	B	19810817		
NL 167692	C	19820118		
IL 49391	A1	19790930	IL 1976-49391	19760412
FR 2308367	A1	19761119	FR 1976-10958	19760414
FR 2308367	B1	19790921		
CA 1059128	A1	19790724	CA 1976-250732	19760414
DD 124599	C	19770302	DD 1976-192399	19760415
GB 1492528	A	19771123	GB 1976-15644	19760415
CS 195726	P	19800229	CS 1976-2549	19760416
JP 51136688	A2	19761126	JP 1976-43763	19760419
JP 55022475	B4	19800617		
ES 447150	A1	19770916	ES 1976-447150	19760419
BE 840904	A1	19760816	BE 1976-166282	19760420
ZA 7602320	A	19771130	ZA 1976-2320	19760420
PL 99664	P	19780731	PL 1976-188912	19760420
SU 638260	D	19781215	SU 1976-2346054	19760420
AT 7602883	A	19790515	AT 1976-2883	19760420
AT 353795	B	19791210		
CH 619468	A	19800930	CH 1976-4926	19760420
RO 73278	P	19820201	RO 1976-85688	19760420
HU 172684	P	19781128	HU 1976-ME1967	19760421
US 4081542	A	19780328	US 1977-774565	19770304
ES 459405	A1	19780816	ES 1977-459405	19770601
ES 459406	A1	19780816	ES 1977-459406	19770601
ES 459407	A1	19780816	ES 1977-459407	19770601

PRIORITY APPLN. INFO.:
US 1975-570052 A 19750421
US 1976-656664 A2 19760209
US 1976-696254 A2 19760615

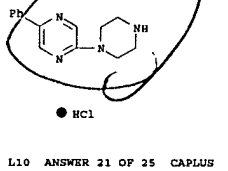
GI



I

AB Appetite-depressing piperazinylpyrazines I (I; R = H, Cl, Ph; R1 = H, Cl, F3C, MeO, PhS, Me2N, MeS; R2 = H, CO2H; R3 = H, Ac) are prepared by various methods. Thus, reaction of piperazine with 2,6-dichloropyrazine in MeCN gives after 90 min at reflux I.HCl (R = R2 = R3 = H, R1 = Cl).

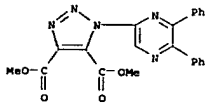
IT 61655-63-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and appetite-depressing activity of)
RN 61655-63-8 CAPLUS
CN Pyrazine, 2-phenyl-5-(1-piperazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



L10 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1971:75924 CAPLUS
DOCUMENT NUMBER: 74:75924
TITLE: Heteroaromaticity. XLIX. Tetrazolo-azido isomerization in heteroaromatics. I. Syntheses and reactivities of some tetrazolopolyazines
AUTHOR(S): Sasaki, Tadashi; Kanematsu, Ken; Murata, Masayoshi
CORPORATE SOURCE: Fac. Eng., Nagoya Univ., Nagoya, Japan
SOURCE: Journal of Organic Chemistry (1971), 36(3), 446-9
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 74:75924

AB The tetrazolo-azido transformation for eight model compds. are discussed. The tetrazolo-azido equilibrium in tetrazolo[1,5-a]pyrazines (I) is much influenced by the solvent, but the tetrazolo[1,5-b]pyridazine derivs. exist entirely as the tetrazoles in various solvents. 6-Azidotetrazolo [1,5-b]pyridazine and 6-azido-s-triazolo[4,3-b]-pyridazine exist exclusively as the azido form in the solid state because of the destabilization of the fused rings by electron attracting tetrazolo and triazolo moieties. Photochem. and thermal reactions of I give the imidazoles.

IT 27062-56-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 27062-56-2 CAPLUS
CN 1H-1,2,3-Triazole-4,5-dicarboxylic acid, 1-(5,6-diphenylpyrazinyl)-, dimethyl ester (8CI) (CA INDEX NAME)

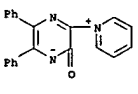


L10 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1962:462756 CAPLUS
DOCUMENT NUMBER: 57:62756
ORIGINAL REFERENCE NO.: 57:12481a-e
TITLE: Reaction of 2-hydroxy-3-nitro-5,6-diphenylpyrazine with pyridine

AUTHOR(S): Ratajczyk, James D.; Carbon, John A.
CORPORATE SOURCE: Abbott Labs., North Chicago
SOURCE: Journal of Organic Chemistry (1962), 27, 2644-5
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Treatment of 5,6-diphenyl-2-hydroxy-3-nitropyrazine (I) with SOCl2 gave 3-chloro-5,6-diphenyl-2-hydroxypyrazine (II), and with POCl3 both II and 2,3-dichloro-5,6diphenylpyrazine (Karmas and Spoerri, CA 48, 175e). In an attempt to obtain normal replacement of the OH group without loss of the NO2 group, 15.0 g. I was treated with 6.0 g. SOCl2 in the presence of 150 ml. dry C5H5N. The mixture kept 18 hrs. before pouring into 335 ml. ice H2O and 165 ml. concentrated HCl and basifying with 45% aqueous KOH, the orange precipitate washed with H2O and the strongly hydrated compound (13.2 g.) dried in vacuo at 100° gave hydrated material, recrystd. from PrOH to give III, m. above 260° (slow decomposition), showing no carbonyl peaks below 6.4 μ, and containing no NO2 group (polarographic determination) III (2.0 g.) refluxed 4 hrs. in 25 ml. 20% H2SO4 and the cooled mixture filtered gave 1.6 g. yellow cryst. solid, recrystd. from AcOH-H2O and dried in vacuo at 100° gave 2,3-dihydroxy-5,6-diphenylpyrazine, m. 340-2° (capillary). The filtrate basified with 50% aqueous NaOH and the filtered solution extracted 3 times with 10 ml. CHCl3, the dried extract concentrated and the residue distilled gave C5H5N. II, (1.2 g.) and 0.50 g. C5H5N.HCl refluxed 2 hrs. in 15 ml. dry C5H5N and the cooled mixture poured into 100 ml. 2N HCl and cracked ice, the solution clarified with Norit and the filtered solution basified with 45% KOH gave 0.25 g. III. I (3.0 g.) heated 1.5 hrs. at 100° in 20 ml. C5H5N and poured into cold dilute HCl, the solution basified and the product crystallized from PrOH gave III. Attempts to prepare III by treatment of II with C5H5N at 100° 2 hrs. or with C5H5N and C5H5N.HCl at 50-60° 2 hrs. gave only recovered II.

IT 100025-56-7, Pyridinium, 1-(3-hydroxy-5,6-diphenylpyrazinyl)-, hydroxide, inner salt
(preparation of)
RN 100025-56-7 CAPLUS
CN 1-(3-Hydroxy-5,6-diphenylpyrazinyl)pyridinium hydroxide, inner salt (7CI) (CA INDEX NAME)

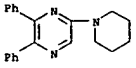


L10 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1957:5526 CAPLUS
DOCUMENT NUMBER: 51:5526
ORIGINAL REFERENCE NO.: 51:1201a-d
TITLE: Heterocyclic N-oxides. Oxides of some diphenylpyrazine derivatives and of 3-nitro- and 7-nitroquinoline
AUTHOR(S): Landquist, Justus K.
CORPORATE SOURCE: Univ. Manchester, UK
SOURCE: Journal of the Chemical Society, Abstracts (1956) 1885-6
CODEN: JCSAAZ; ISSN: 0590-9791
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 51:5526

AB 3-Nitroquinoline (I) and 7-nitroquinoline (II) treated with

monoperphthalic acid (III) gave 3-nitroquinoline N-oxide (IV) and 7-nitroquinoline N-oxide (V), resp. I (8.7 g.) in 60 cc. dry dioxane added during 10 min. to an ice-cold solution of II in Et2O after 3 days gave 4.5 g. unchanged I and 0.5 g. IV, as crystals, m. 192-3°. IV was obtained by oxidation with 1.2M peracetic acid (VI) at 50° overnight. II (5 g.) in dioxane similarly left 5 days with 25% excess III yielded 1.6 g. V, yellow crystals, m. 174-5° (from C6H6 and then MeOH). 2,3-Diphenylpyrazine (VII) with VI gave 2,3-diphenylpyrazine 1-oxide (VIII) and 2,3-diphenylpyrazine 1,4-dioxide (IX). Thus 5.8 g. VII and 80 cc. 1.2M VI heated overnight at 50° gave 2.9 g. VIII as needles, m. 171-2°, and the aqueous filtrate made alkaline gave 2 g. IX, platelets, m. 262° (decomposition) (from EtOH). By using similar oxidation conditions the following were prepared: 5,6-dihydro-2,3-diphenylpyrazine 1,4-dioxide, needles, m. 244° [from EtO(CH2)2OH] and 2,6-diphenylpyrazine 5(7)-oxide, needles, m. 200-1° (from alc.). VIII (1.6 g.) and 6 cc. POCl3 refluxed 20 min. and poured on ice gave 1.7 g. 2-chloro-5,6-diphenylpyrazine (X), prisms, m. 125-6° (from cyclohexane). X (2.6 g.) and 9 cc. piperidine refluxed 1.5 hrs. and poured into H2O yielded 5,6-diphenyl-2-piperidinopyrazine (2.4 g.), m. 127-9° (from alc.). Oxidation of quinazoline with VI gave 4-hydroxyquinazoline. It is probable that some compds. described in the literature as N-oxides are C-hydroxy compds. These may be distinguished from N-oxides by their high m.p., solubility in aqueous NaOH, and sparing solubility in organic solvents.

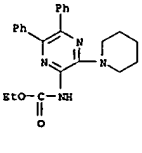
IT 102659-57-4, Pyrazine, 2,3-diphenyl-5-piperidino-
(preparation of)
RN 102659-57-4 CAPLUS
CN Pyrazine, 2,3-diphenyl-5-piperidino- (6CI) (CA INDEX NAME)



L10 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1954:25073 CAPLUS
DOCUMENT NUMBER: 48:25073
ORIGINAL REFERENCE NO.: 48:4553h-i,4554a-i,4555a-d
TITLE: Pteridines. X. A new approach to the synthesis of pteridines
AUTHOR(S): Taylor, E. C., Jr.; Carbon, John A.; Hoff, Dale R.
CORPORATE SOURCE: Univ. of Illinois, Urbana
SOURCE: Journal of the American Chemical Society (1953), 75, 1904-8
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S):. CASREACT 48:25073
GI For diagram(s), see printed CA Issue.
AB cf. C.A. 48, 2719c. A new synthesis of pteridines is described involving the preliminary synthesis of a 2,4(1H,3H)-pteridinedione (lumazine) by the conventional method and the subsequent aminolytic cleavage of the pyrimidine portion of the lumazine to give a 3-amino-N-substituted pyrazinamide, followed by its ring closure to the desired pteridine. This method permits a much wider variation in the structure of the pyrimidine ring than does the conventional approach. Dry freshly distilled BuNH2 (100 cc.) and 15 g. 6,7-diphenyl-2,4(1H,3H)-pteridinedione (I) heated 12 h. in a sealed tube at 180°, the clear light brown solution treated with Norit, the excess BuNH2 removed in vacuo, and the residue diluted with 50 cc. hot EtOH and then hot H2O to incipient crystallization gave 8.8 g. (53.3%) 3-amino-N-butyl-5,6-diphenylpyrazinamide (II), bright yellow prisms, m. 146-7° (from CHCl3-aqueous EtOH). 3-Amino-N-benzyl-5,6-diphenylpyrazinamide (0.520 g.) in 20 cc. HC(OEt)3 (III) and 20 cc. Ac2O refluxed 5 h., and the solution evaporated to dryness in vacuo yielded 0.386 g. (72.3%) 3-benzyl-6,7-diphenyl-4(3H)-pteridinone (IV), white platelets, m. 248° (from CHCl3-petr. ether). II (1.0 g.) in 20 cc. 98-100% HCO2H and 20 cc. Ac2O refluxed 5 h., and the clear light yellow solution evaporated repeatedly to dryness in vacuo with 50-cc. portions of EtOH gave 0.337 g. (32.8%) 3-Bu analog (V) of IV, white platelets, m. 194-5° (from CHCl3-aqueous EtOH). II (0.50 g.), 20 cc. III, and 20 cc. Ac2O refluxed 5 h. similarly gave 0.396 g. (77%) V. 3-Amino-N-benzyl-5,6-diphenylpyrazinamide (1.0 g.) and 25 cc. ClCO2Et (VI) refluxed 20 h., and the resulting clear yellow solution evaporated repeatedly to dryness with 50-cc. portions of EtOH gave 0.996 g. (93.7%) N-benzyl-3-carbethoxyamino-5,6-diphenylpyrazinamide (VII), colorless prisms, m. 129-30° (from CHCl3-petr. ether). II (2.0 g.), and 40 cc. VI refluxed 20 h. gave similarly 1.539 g. (63.7%) N-Bu analog (VIII) of VII, colorless prisms, m. 110-11° (from CHCl3-petr. ether). VII (0.574 g.) and alc. NaOEt (from 0.5 g. Na in 70 cc. absolute EtOH) refluxed 20 h. gave 0.211 g. (40.9%) 3-benzyl-6,7-diphenyl-2,4(1H,3H)pteridinedione (IX), long colorless needles, m. 194-5° (from CHCl3-petr. ether). VIII (1 g.) similarly gave 0.80 g. (88.8%) 3-Bu analog of IX, long white needles, m. 246-7° (from CHCl3-petr. ether). 3-Amino-N-benzyl-5,6-diphenylpyrazinamide (X) (0.597 g.) and 25 cc. HCONH2 heated 3 h. at 190°, and the mixture cooled and diluted with H2O yielded 0.304 g. (64%) 6,7-diphenyl-4(3H)-pteridinone (XI), m. 297-8° (from aqueous HCONMe2), also obtained by refluxing X with HCONH2 containing 2 cc. dilute HCO2H. II similarly gave 52% XI. Me 3-amino-5,6-diphenylpyrazinoate (0.856 g.) in 75 cc. MeOH saturated with anhydrous NH3 at 0° and heated 1 h. at 120° in a sealed tube yielded 0.700 g. (86%) 3-amino-5,6-diphenylpyrazinamide (XII), m. 204-5° (from aqueous EtOH). XII (0.529 g.), 1.0 g. P2S5, and 15 cc. dry pyridine refluxed 1 h., the deep red solution cooled, poured into 200 cc. H2O, the resulting orange colloidal suspension dissolved by the addition of a small amount of 10% NaOH, the solution treated with C, filtered, and the filtrate acidified with glacial AcOH gave 0.304 g. (54.6%) 3-amino-5,6-diphenylthiopyrazinamide (XIII), orange needles, m. 158-60° (from aqueous EtOH). XI (2.975 g.), 4 g. P2S5, and 50 cc. anhydrous pyridine refluxed 2 h. similarly gave 2.34 g. (75%) 6,7-diphenyl-4(3H)-pteridinethione (XIV), bright red platelets, m. 270-80° (decomposition) (from aqueous HCONMe2). XIII (0.286 g.) in 10 cc. III and 10 cc. Ac2O refluxed 5 h. gave 0.164 g. (55.4%) XIV, bright red shiny platelets. XIV (0.5 g.), 1 cc. PhCH2NH2, 1 g. HgO, and 30 cc. EtOH refluxed 5 h., the mixture filtered, the black residue washed with 10 cc. hot EtOH, and the filtrate combined with the washings and diluted with H2O until crystallization began yielded 0.61 g. (99%) 4-benzylamino-6,7-diphenylpteridine (XV), light yellow platelets, m. 178-9° (from aqueous Me2CO). XIV (0.951 g.), 1.5 cc. BuNH2, 1 g. HgO, and 20 cc. absolute EtOH refluxed 2.5 h. similarly gave 0.870 g. (74.3%) N-Bu analog (XVI) of XV, bright yellow plates, m. 150-1° (from aqueous EtOH). XIV (2.0 g.) and 50 cc. absolute EtOH saturated with NH3 at 0° and heated in a sealed tube 10 h. at 130° gave 1.59 g. (84%) 4-amino-6,7-diphenylpteridine, light yellow needles, m. 175° (from aqueous Me2CO). Refluxing 0.924 g. XIV in 5 cc. CHCl3 and 20 cc. absolute EtOH with 0.8 g. HgO yielded 0.414 g. (33%) mercuric salt of XIV, light yellow crystals, m. 268-71° (from CHCl3-absolute EtOH). XV (0.20 g.) in 10 cc. 6N HCl refluxed 0.5 h. and the cooled mixture neutralized with NH4OH gave 0.14 g. (93%) XI, m. 297-8°. XI (88%) was also formed by hydrolysis of XVI. II (1.75 g.), 2.0 g. P2S5, and 25 cc. dry pyridine refluxed 1 h., the mixture cooled, poured into 150 cc. H2O, and the precipitate washed with H2O and recrystd. from absolute EtOH gave 1.54 g. (83.4%) 3-amino-N-butyl-5,6-diphenylthiopyrazinamide (XVII), bright yellow needles, m. 168-9°. XVII (0.635 g.), 0.7 g. freshly fused NaOAc, 10 cc. 98-100% HCO2H, and 10 cc. Ac2O refluxed 5 h. gave 0.441 g. (67.6%) 3-butyl-6,7-diphenyl-4(3H)-pteridinethione (XVIII), orange needles, m. 193-5° (from CHCl3-EtOH). XVII (1.53 g.) in 10 cc. HC(OEt)3 and 10 cc. Ac2O refluxed 3 h. yielded 0.962 g. (61.2%) XVIII. XVII (1.139 g.) in 30 cc. ClCO2Et refluxed 20 h., the solution evaporated to dryness in vacuo, and the residue evaporated 3 times with 50-cc. portions of absolute EtOH yielded 1.11 g. (77%) carbethoxy derivative (XIX), microcryst. orange solid, m. 173-4° (from CHCl3-EtOH). XIX heated 15 min. with 5 cc. 10% aqueous NaOH in 20 cc. EtOH gave 73% 1,2-dihydro-2-oxo derivative of XVIII, orange-red solid, m. 205-9° (from aqueous EtOH). XVIII (0.179 g.) in 1.5 cc. CHCl3 and 10 cc. absolute EtOH refluxed 6 h. with 0.2 g. HgO while a continuous stream of NH3 was passed through the mixture, the mixture filtered hot, and the filtrate evaporated to a small volume deposited 0.119 g. (69.8%) 3-butyl-4(3H)imino-6,7-diphenylpteridine, yellow platelets, m. 149-51°.

3-Amino-5,6-diphenylpyrazinoic acid piperidide (1.50 g.) in 50 cc. VI refluxed 5 h. and the mixture worked up in the usual manner gave 1.42 g. (79%) 3-carbethoxyamino-5,6-diphenylpyrazinoic acid piperidine (XX), yellow platelets, m. 174-5° (from aqueous Me2CO and then CH2Cl2-petr. ether). XX (0.50 g.) in 40 cc. EtOH saturated with dry NH3 and heated 6 h. in a sealed tube at 155°, the solution evaporated to dryness, the residue dissolved in dilute NH4OH, and the solution acidified with glacial AcOH gave 0.330 g. (90%) I, colorless microcryst. solid, m. 320-5°.

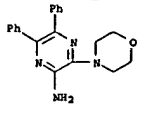
IT 857374-73-3, Piperidine, 1-(3-carboxyamino-5,6-diphenylpyrazinoyl)-, ethyl ester
(preparation of)
RN 857374-73-3 CAPLUS
CN Piperidine, 1-(3-carboxyamino-5,6-diphenylpyrazinoyl)-, ethyl ester (5CI) (CA INDEX NAME)



L10 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1954:3618 CAPLUS
DOCUMENT NUMBER: 48:3618
ORIGINAL REFERENCE NO.: 48:688c-i,689a
TITLE: Aminolysis of heterocyclic amides. I. The aminolysis of 6,7-diphenyllumazine
AUTHOR(S): Taylor, E. C., Jr.
CORPORATE SOURCE: Univ. of Illinois, Urbana
SOURCE: Journal of the American Chemical Society (1952), 74, 1651-5
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. following abstract An alkylamine with 6,7-diphenyllumazine (I) gives first an N-substituted amide of a 3-(3-alkylureido)-5,6-diphenylpyrazinoic acid, which can then be converted to an N-substituted amide of 3-amino-5,6-diphenylpyrazinoic acid by further reaction with the amine. The mechanism of these transformations is discussed and the results are interpreted as a substantiation for the ring cleavages previously postulated (cf. C.A. 47, 137h) in the reaction of 4-NH2 and 4-hydroxy-2-mercaptopteridines with alkylamines. I (3.0 g.) in 20 cc. PhCH2NH2 (II) refluxed 15 min. and diluted with 50 cc. absolute EtOH yielded 2.18 g. N-benzyl-3-(3-benzylureido)-5,6-diphenylpyrazinamide (III). EtOH, m. 88-93°; III m. 150-1°. III (0.60 g.), 10 cc. Ac2O, and 3 g. NaOAc refluxed 2 h., and the cooled mixture poured on ice and let stand overnight yielded III, m. 150-1°. III (0.50 g.) in 10 cc. II refluxed 8 h., diluted with 20 cc. EtOH, heated to boiling and diluted with water to incipient precipitation yielded 0.348 g. 3-amino-N-benzyl-5,6-diphenylpyrazinamide (IV), m. 188.5-9°; the filtrates from IV concentrated to 20 cc. and diluted with 20 cc. water yielded N,N'-dibenzylurea (V), 168°. I and II refluxed 8 h. yielded directly IV and V. H2SO4 (2 cc.) added slowly to 1.0 g. 3-amino-5,6-diphenylpyrazinoic acid in 15 cc. absolute EtOH, the solution let stand 24 h. at room temperature, and poured into 75 cc. water yielded 0.91 g. Me ester (VI), m. 204-6°. VI (165 mg.) and 2 cc. II refluxed 10 min., diluted with 15 cc. 50% EtOH and cooled yielded 190 mg. IV, m. 188.5-89°. IV (1.0 g.), 20 cc. 85% HCO2H, 20 cc. Ac2O, and 1.0 g. NaOAc refluxed 5 h. and the solution evaporated to dryness yielded 0.42 3-benzyl-6,7-pteridin-4(3H)-one, m. 248°. I (0.50 g.) and 15 cc. morpholine refluxed 14 h. yielded 0.53 g. 3-(morpholinocarbonylamino)-5,6-diphenylpyrazinoic acid morpholide (VII), m. 262-4°. VII (1.0 g.) sealed in 20 cc. morpholine heated 12 h. at 140° and 6 h. at 190° yielded 0.64 g. 3-amino-5,6-diphenylpyrazinoic acid morpholide (VIII), m. 190.5-1°. I and morpholine heated 12 h. at 190° yielded VIII directly. I (3.0 g.), 30 cc. piperidine, and 10 cc. HCONMe2 refluxed 16 h., filtered, and the hot filtrate treated with boiling water to incipient turbidity yielded 1.67 g. 3-(piperidinocarbonylamino)-5,6-diphenylpyrazinoic acid piperidide, m. 215-17°. I (5.0 g.) in 50 cc. piperidine heated 20 h. at 200° yielded 3.8 g. 3-amino-5,6-diphenylpyrazinoic acid piperidide, m. 156°. I (0.50 g.) in 15 cc. HOCH2CH2NH2 refluxed 12 h. yielded 0.453 g. 3-amino-N-(β-hydroxyethyl)-5,6-diphenylpyrazinamide, m. 186.5-87°. I (2.0 g.) and 40 cc. NH4OH heated 16 h. at 185° yielded 1.67 g. 3-amino-5,6-diphenylpyrazinamide (IX), m. 203.5-5°. IX (0.3 g.) and 1 cc. II refluxed 15 min., diluted with 10 cc. EtOH, and hot water added to incipient crystallization yielded 0.31 g. IV. IX (0.06 g.), 5 cc. piperidine, and 2 cc. HCONMe2 refluxed 16 h. yielded 0.053 g. IX, m. 203.5-5°. p-O2NC6H4NHCONH2 (2.0 g.) and 20 cc. piperidine refluxed 8 h. yielded 2.43 g. 1-(p-nitrophenyl)-3-(piperidino)urea, m. 165-6°. I (1.0 g.) and 10 cc. 85% H4N2.H2O refluxed 6 h. and the mixture let stand 3 h. at 0° yielded 0.705 g. 3-amino-5,6-diphenylpyrazinoic acid hydrazide (X), m. 250-1°. The mother liquors from X evaporated to dryness, the residue washed with water, dried, extracted with CH2Cl2, and the extract diluted with petr. ether yielded 3-amino-6,7-diphenyl-2,4(1H,3H)-pteridinedione, m. 259-60° (decomposition); evaporation of the filtrates yielded about 0.015 g. X.

IT 859822-86-9, Morpholine, 4-(3-amino-5,6-diphenylpyrazinoyl)-
(preparation of)
RN 859822-86-9 CAPLUS
CN Morpholine, 4-(3-amino-5,6-diphenylpyrazinoyl)- (5CI) (CA INDEX NAME)

NO GOOD - CAN'T HAVE TWO Ph's.



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